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THE HEMODYNAMOGRAM: FETAL, NORMAL, AND ABNORMAL BLOOD CIRCULATION DEPICTED BY A NEW METHOD

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THIS method for the depiction of the blood circulation has grown out of a study now being conducted on congenital heart disease at The Children's Hospital, Washington, D. C. With the advent of the newer diagnostic methods now being used in the investigation of congenital cardiac lesions, it was felt that some simple method should be evolved which would readily lend itself to a rapid visualization of the circulatory defects as they were determined. The line diagrams to be presented here have all been constructed from, and pertain to, patients who have come to autopsy at this hospital.

THE NORMAL HEMODYNAMOGRAM

The name hemodynamogram has been arbitrarily assigned to our depiction of the blood circulation, and in this and in all following instances will be referred to as the fetal, normal, or abnormal hemodynamogram. For purposes of simplification, the hemodynamogram has been depicted as a figure-of-eight. This is shown in Fig. 1. On inspection of this diagram, it may be seen that the course of blood flow may be followed as a continuous process rather than as two separate circulations. The pulmonary and the systemic circulations have been labeled Cycles "A" and "B" respectively. The whole circulation might just as easily have been represented as one large circle; however, in view of the congenital anomalies encountered, the figure-of-eight pattern is much more easily adapted to simplification of explanation.

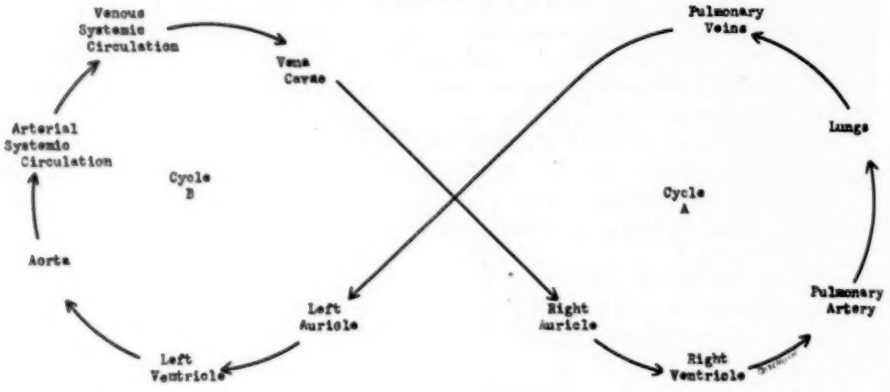
FETAL BLOOD CIRCULATION—FETAL HEMODYNAMOGRAM

For sake of completeness, there is included a description of the fetal blood circulation before the changes occur which are attendant upon parturition.

As can be seen by an inspection of Fig. 2, the fetal circulation is grossly the same as in the adult with the exception that there are a number of circuitous pathways by which the blood travels in order to circumvent a nonfunctioning organ (the lung) and to receive oxygen and expel carbon dioxide (placental circulation).

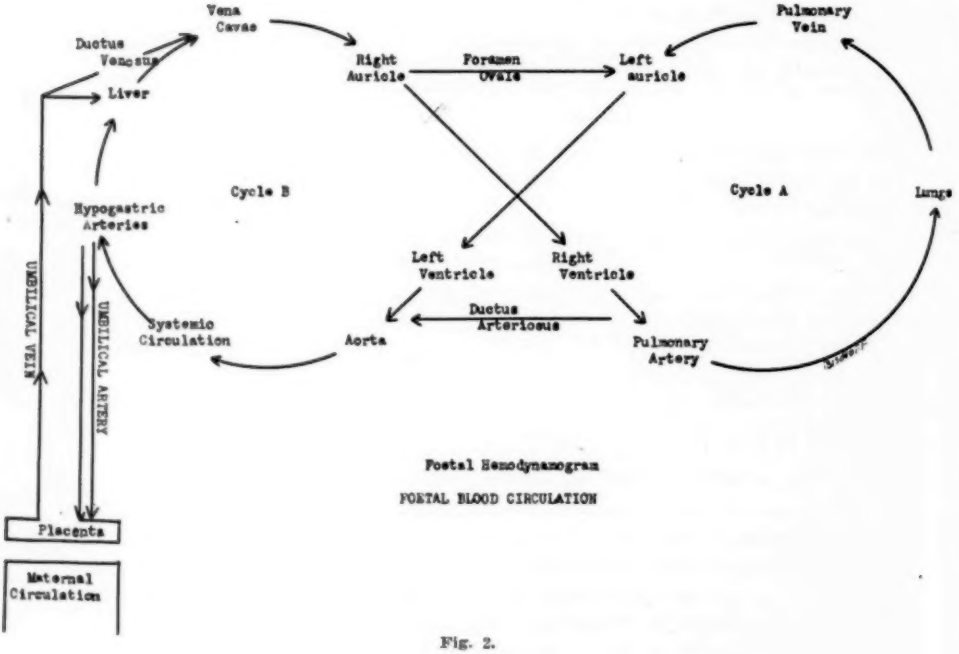
From the Department of Pathology, The Children's Hospital, Washington, D. C.

Fig. 1.



Normal Hemodynamogram

NORMAL BLOOD CIRCULATION



Foetal Hemodynamogram

FOETAL BLOOD CIRCULATION

Fig. 2.

A part of the blood coming into the right auricle is passed through the foramen ovale to the left auricle, whence it eventually passes out over the systemic circulation. Upon coming to the common iliac vessels, a portion of the blood is sent to the placenta by way of the hypogastric and umbilical arteries and is returned from the placenta through the umbilical vein. The blood passes mostly to the inferior vena cava through the ductus venosus. A certain proportion of the blood is not passed through the foramen ovale but passes in normal fashion into the pulmonary artery. Shortly after entering the pulmonary artery, the blood encounters another shunt, the ductus arteriosus. By this route blood from the pulmonary artery is sent into the aorta and thence to the systemic circulation.

By these pathways, a minimum of blood is sent through the lungs. The atelectatic or pre-expansive state of the lungs assists in maintaining this circulation by virtue of the resistance offered by narrowed blood capillaries. When birth occurs, the sudden or at least partial expansion of the lung tissue removes the resistance holding back the passage of blood through the lung capillaries, and an approximation to adult circulation is initiated.

Then, granting a normal embryologic development of the septa primum and secundum, with an increased pressure within the left ventricle, the foramen ovale becomes functionally closed.

Christie in 1930[1] reviewed the literature on the closing time of the foramen ovale and the ductus arteriosus and found the statements to be markedly controversial. In a review of consecutive autopsies, excluding all congenitally malformed hearts, he found the closing time of the foramen ovale to be prior to twelve weeks after birth in 87 per cent of 590 normal hearts of infants from one day to one year of age. Likewise he found the closure of the ductus arteriosus to occur prior to eight weeks after birth in 88 per cent of 588 normal hearts of infants from one day to one year of age.

THE ABNORMAL HEMODYNAMOGRAM

In order to demonstrate the clearness of the proposed method, we have included a classical diagram drawn to represent a case of transposition of the great vessels according to the method used by Maude Abbott,[2] in order that the reader may compare the advantage of the newer method (Fig. 3).

Fig. 4 shows the representation by the hemodynamogram method of transposition of the great vessels. It becomes readily apparent that, by transposition of the great vessels, the systemic and the pulmonary circulations become independent of each other, and were the by-pass defects noted not present, the condition would be entirely incompatible with life.

Patent Ductus Arteriosus (*Fig. 5*).—The ductus arteriosus originates from the pulmonary artery at the bifurcation of the two main branches and connects with the aorta beyond the origin of the left subclavian artery. In one child who was proved at autopsy to have an Eisenmenger complex[3] the left subclavian artery arose from the middle of the ductus arteriosus. That portion of the

ductus which communicated with the left subclavian artery was of the same inside diameter as the latter vessel and opened into the aorta, while the ductus on the pulmonary artery side was entirely occluded.

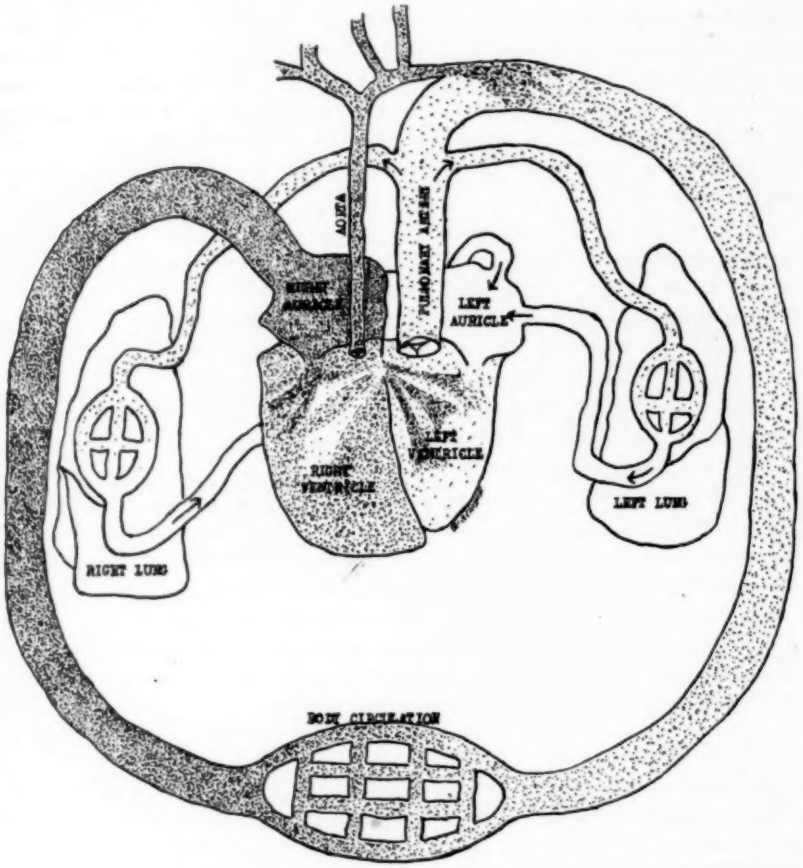
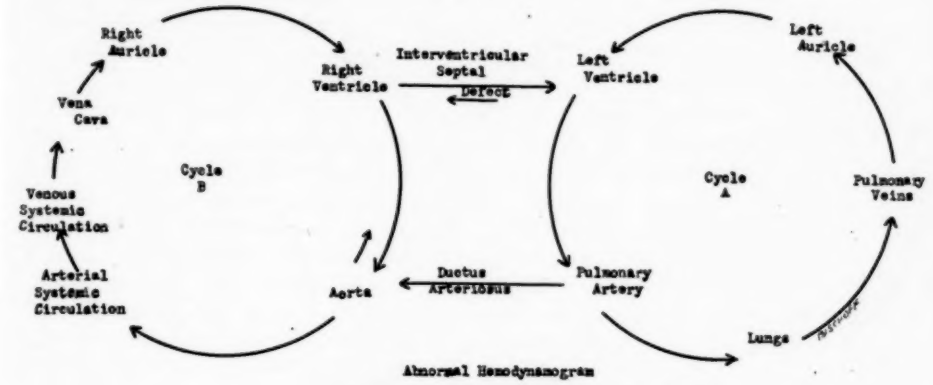


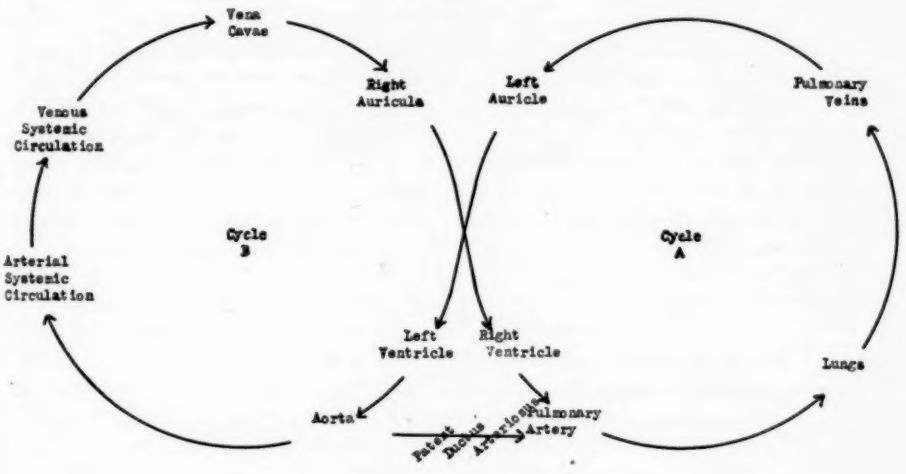
Fig. 3.—Transposition of great vessels, interventricular septal defect, patent ductus arteriosus aortic stenosis.

When the ductus arteriosus remains patent, due to the higher pressure in the aorta, blood passes from that vessel into the pulmonary artery. This is represented in Fig. 5 by an arrow passing from Cycle A to Cycle B. Hence oxygenated blood passes from the systemic to the pulmonary circulation, and in the absence of any increased pressure in Cycle B, no cyanosis is produced.

Fig. 4.



BLOOD CIRCULATION IN TRANSPOSITION OF THE GREAT VESSELS WITH PATENT DUCTUS ARTERIOSUS AND INTERVENTRICULAR DEFECT. CASE OF R. W.



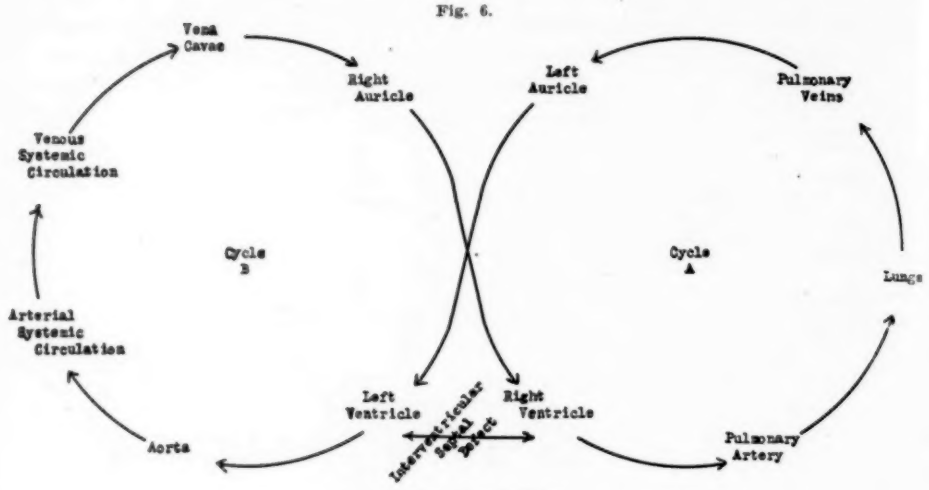
ABNORMAL HEMODYNAMOGRAM

PATENT DUCTUS ARTERIOSUS, CASE OF L.W.

Fig. 5.

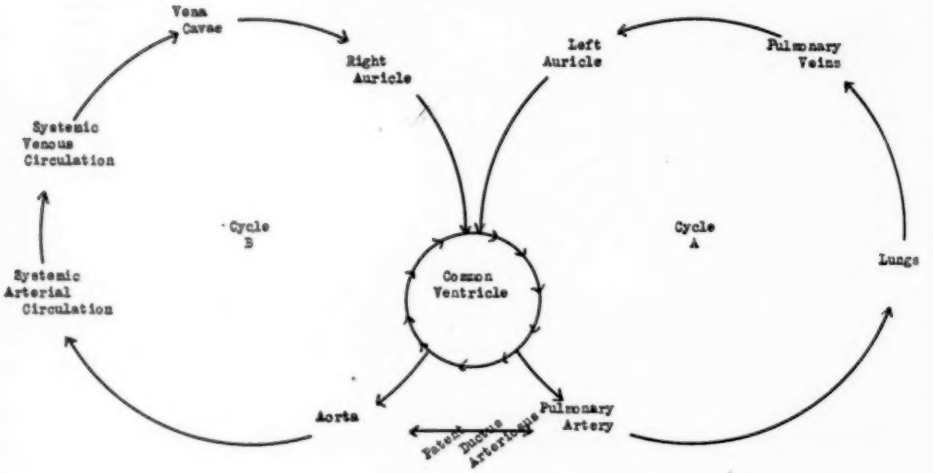
Interventricular Septal Defect (*Fig. 6*).—In the case of the interventricular septal defect we have almost the same situation as we have with patency of the ductus arteriosus. Here blood is passed from the left ventricle to the right ventricle. As stated by Taussig,[4] cyanosis never occurs in a maladie de Roger, since blood will always pass from an area of high pressure to one in which the pressure is low. We have indicated the flow of blood in both directions only to satisfy the theoretical anatomic possibility of that event.

Fig. 6.



ABNORMAL HEMODYNAMOGRAM

INTERVENTRICULAR SEPTAL DEFECT, BICUSPID AORTIC VALVE, CASE OF H.O.



ABNORMAL HEMODYNAMOGRAM

COR TRILOCULARE BIATRIATUM, PATENT DUCTUS ARTERIOSUS, CASE OF K.B.

Fig. 7.

Cor Triloculare Biatriatum (Fig. 7).—In this condition there is mixing of arterial and venous bloods in the common ventricle so that blood reaching the systemic circulation is only partially saturated with oxygen. Blood passing out of the common ventricle would be of the same pressure in both the aorta

and pulmonary artery; hence, although in the case illustrated, a patent ductus arteriosus was present, this would in no way influence the passage of blood from the aorta to the pulmonary artery or vice versa. The arrow depicting the passage of blood between the aorta and pulmonary artery has been drawn to depict the passage of blood in either direction. With presumably identical pressure in both trunks, the passage of blood through the ductus should be subject to variation according to the variations in intrathoracic pressure.

Truncus Arteriosus Communis Persistens (Fig. 8).—The drawing shown in Fig. 8 shows the circulation in two cases of truncus arteriosus communis persistens[5] in which there were in addition to the common truncus, interauricular septal defects. The arrow between the auricles designates the flow of blood in both directions. In one of our patients there were multiple perforations and in the other the perforation was single. It is rather difficult to believe that in the presence of multiple perforations the flow of blood would be in only one direction, especially since blood would enter both circulations at the same pressure. This equality of pressure must certainly be reflected onward through both Cycles A and B.

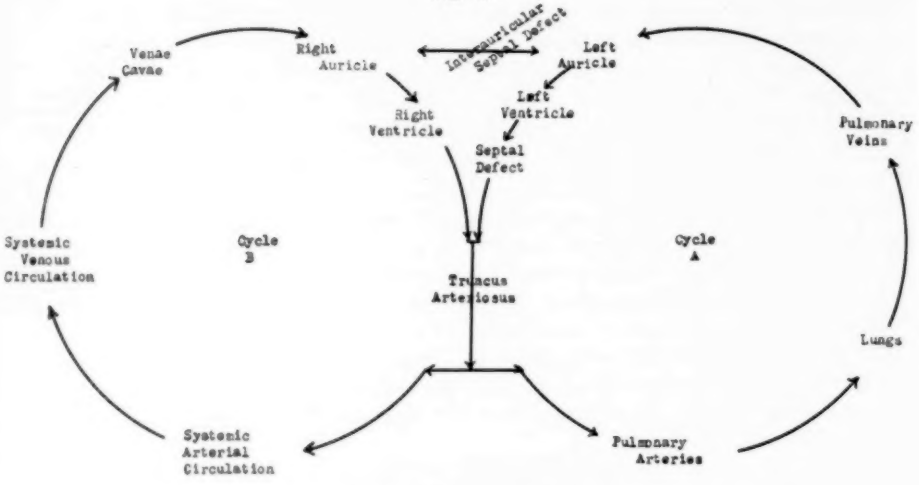
Cor Triloculare Biatriatum—Atresia of Pulmonary Artery (Fig. 9).—This figure is similar to Fig. 7; however there is, in addition to the cor triloculare, a patency of the foramen ovale and an atresia of the pulmonary artery. In this child the blood supply to the lungs was effected through the bronchial arteries, which were dilated and tortuous. In this case, the bronchial arteries were much smaller than the aorta. A fluid passing through a smaller tube, or, as in this case, an artery, will pass at a greater rate of speed, and the pressure will drop in proportion to the size of the tube. Considering the latter fact, plus the normal drop in pressure, one would expect blood from Cycle B to enter Cycle A through the patent foramen ovale. The theoretical possibility always remains, however, that blood may pass in either direction; hence the arrow is drawn to depict blood passing in either direction.

Cor Triloculare Biatriatum—Mitral Aplasia—Interauricular Septal Defect (Fig. 10).—In this situation we have, in addition to the cor triloculare, a mitral aplasia and a patent ductus arteriosus. Although anatomically a three-chambered heart, functionally it was two-chambered. Due to the mitral aplasia, all blood returning from Cycle A to the left auricle was passed directly into the right auricle by way of the interauricular septal defect. After passing into the common ventricle it was distributed to the aorta and pulmonary artery. With presumably the same pressure in both of the latter vessels, blood might well pass in either direction between them.

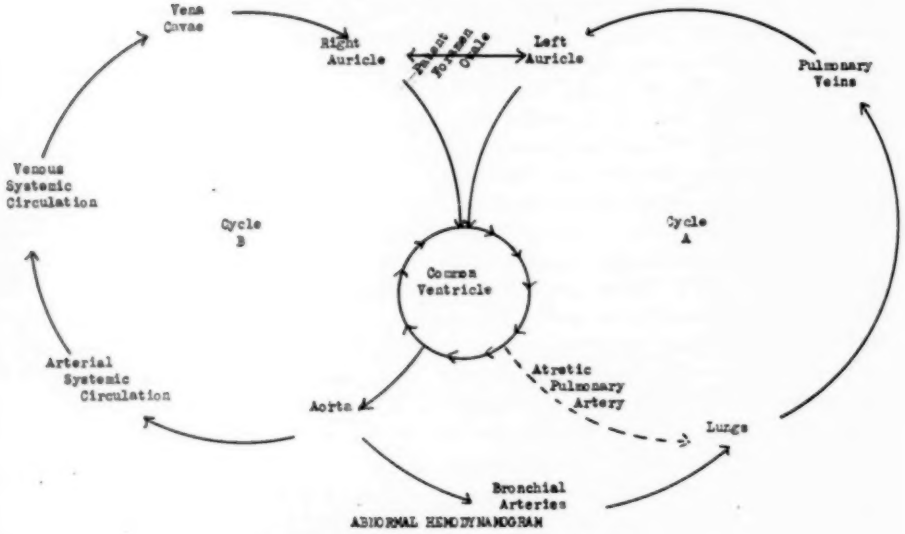
Persistent Ostium Atrioventriculare Commune (Fig. 11).—The last abnormal hemodynamogram to be shown is that of a child with persistent ostium atrioventriculare commune.

In the case illustrated, the interauricular septum came down to the common valve and probably did not allow for any great amount of mixing of blood. However since the defect did exist, during certain stages of the cardiac cycle there must have been mixture of arterial and venous blood. The absence of

Fig. 8.



ABNORMAL HEMODYNAMOGRAM
TRUNCUS ARTERIOSUS COMMUNIS PERSISTENS, CLOSED FORAMEN OVALE, ABSENT DUCTUS ARTERIOSUS, INTERVENTRICULAR SEPTAL DEFECT, INTERAURICULAR SEPTAL DEFECT. CASES R.M. AND C.S.

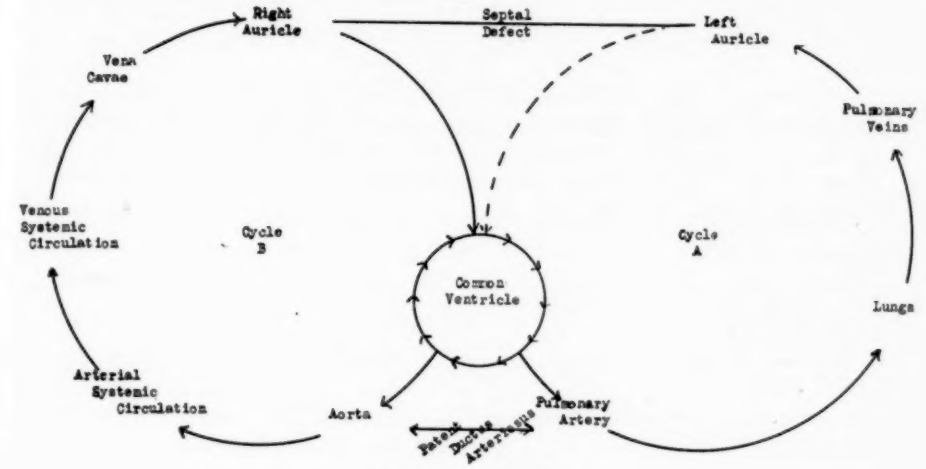


ABNORMAL HEMODYNAMOGRAM

COR TRILOCULARE BIATRIATUM, PATENT FORAMEN OVALE, ATRESIA OF PULMONARY ARTERY, CASE OF J.B.

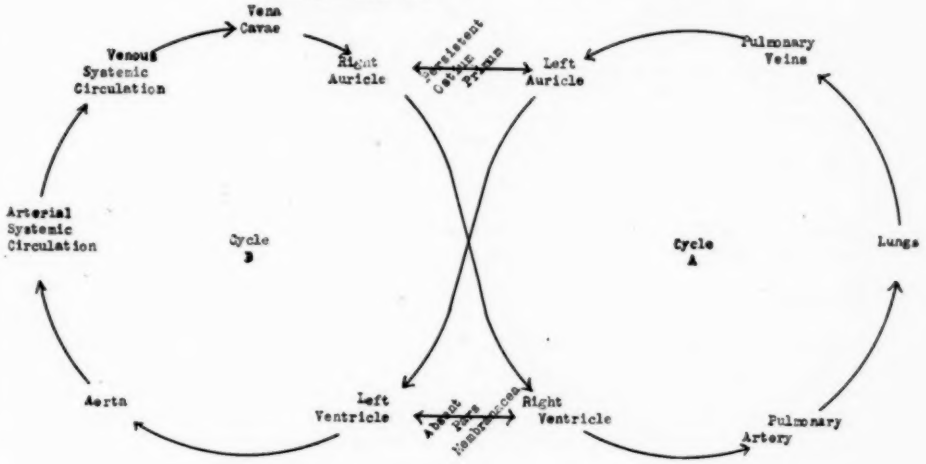
Fig. 9.

Fig. 10.



ABNORMAL HEMODYNAMOGRAM

COR TRILOCULARE BIATRIATUM, CLOSED FORAMEN OVALE, INTER-AURICULAR SEPTAL DEFECT, PATENT DUCTUS ARTERIOSUS, MITRAL APLASIA, CASE OF C.C.



ABNORMAL HEMODYNAMOGRAM

PERSISTENT OSTIUM ATRIO-VENTRICULARE COMMUNE, BILOCULATE HEART. CASE OF C.E.J.

Fig. 11.

the pars membranacea gave rise to further possibility for mixing of arterial and venous blood, and since it was of large size, no doubt allowed passage in both directions.

SUMMARY AND CONCLUSIONS

The normal, fetal, and abnormal hemodynamogram is presented. Minor or major differences in the different hearts have required variations in the schematic diagrams presented. The over-all picture of the circulation, however, is represented by a figure-of-eight, with the pulmonary cycle designated as Cycle A and the systemic cycle as Cycle B.

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TRUNCUS ARTERIOSUS COMMUNIS PERSISTENS

A Report of Three Cases

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THE controversial subject of the requirements which a particular pathologic specimen should meet before it may be classed as a "true" truncus arteriosus has been quite satisfactorily settled by Taussig.[1]

Of the three cases to be presented, in two there were four cusps guarding the common trunk, while in the other there were only three. In all three of the cases the coronary arteries arose from the common trunk; in two the pulmonary and the systemic arteries were both derived from the common trunk. In the other case the truncus had been cut off before any of its branches were given off, and it was therefore impossible to determine accurately the ultimate course of the branches.

There was no ductus arteriosus observed in any of the three cases.

The youngest child was 16 days old, the second 2 months, and the oldest 8 months. All three were male infants.

CASE REPORTS

Case 1.—P. de F., aged 8 months, was born following a normal pregnancy and an eleven-hour labor. The child was placed in an oxygen tent for the first twenty-four hours of life because of his poor color. The child was taken home at 5 days of age and was said to have had blue fingernails, rapid respirations, and a rapid heart rate at that time. At 5 weeks of age the child was fluoroscoped and x-rayed. The mother was told at that time that her child had an enlarged heart. X-ray therapy to the thymus did not reduce the supracardiac shadow.

The parents were told to prevent the child from crying. As a result the child had been either held or carried eighteen to twenty hours a day. When crying the child became rather dusky, but did not become as blue as he had when he was 5 months of age.

The patient was digitalized at 3 months of age, and he was continued on a maintenance dosage of 5 drops of tincture of digitalis until his death at 8 months of age.

Six days before entry into Children's Hospital, the child was taken to a convalescent home for the purpose of training. While there he was a problem to the nursing staff, and three days after entry he had a "temper tantrum," which did not serve to ameliorate his cardiac condition. Eight to ten hours before entry into The Children's Hospital the patient had a temperature of 102° F. and had five or six clay-colored, watery stools.

The family history was noncontributory.

Physical examination revealed a poorly developed and nourished white male infant 8 months of age. The skin was pale, and there was a marked lack of subcutaneous fat. There was a slight duskiness to the skin. There were scattered râles over both lung fields and a respiratory rate of 28 to 34 per minute. The heart was enlarged to the right and left. The rate was regular and greater than 200 per minute. There were loud heart sounds at the apex with a harsh blowing systolic murmur, which was maximal at the apex. There was also a slapping P_2. The remainder of the physical examination was negative.

From the Departments of Pediatrics and Pathology, The Children's Hospital, Washington, D. C.

A hemogram on admission showed 16 Gm. of hemoglobin, 6.4 million red blood cells, and 14 thousand white blood cells, with 46 per cent neutrophiles and 54 per cent lymphocytes. Urinalysis revealed 100 mg. of albumin, many hyaline casts, rare coarse and fine granular casts, and an occasional white blood cell. The urine specimen was of insufficient quantity for the determination of specific gravity.

The day after entry the temperature rose to 105.4° F., the heart rate was over 200, and there were very rapid, deep respirations. There were eight liquid, greenish yellow stools in twenty-four hours. The child was placed in an oxygen tent but expired twelve hours later.

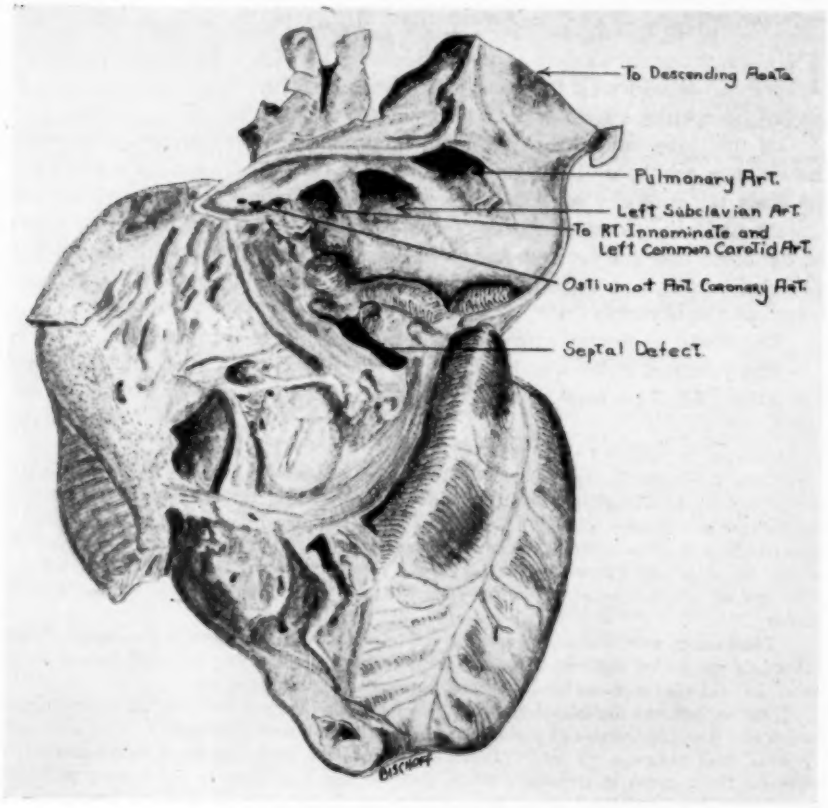


Fig. 1.—Truncus arteriosus communis.

Post-Mortem Findings.—

The body was that of a fairly well developed but poorly nourished white male infant. There was a dearth of subcutaneous fat.

The skull was grossly normal with no unusual prominences or bossing. There was considerable vascular congestion over the convex surface of the brain. The vessels at the base showed no abnormalities. The gyri and sulci appeared to be within normal limits. There was some edema of the meninges. Upon coronal section of the brain, the ventricular system was found to be within normal limits.

The thymus weighed 12 Gm., was pink in color, and soft in consistency. No enlargement was noted of the mediastinal or bronchial lymph nodes; the trachea and bronchi were patent

and grossly normal. The right lung was voluminous, boggy, and contained air. The cut surface was a light red color, and the bronchioles were filled with a pinkish, serous fluid. The left lung was partially collapsed, contained no air, was a dark purple in color, and rubbery in consistency. The cut surface of the left lung was dark purple in color, and no fluid could be expressed from it.

There were approximately 15 c.c. of straw-colored fluid in the pericardial sac. The heart was tremendously enlarged, mostly to the left, and the left lung was compressed by the enlarged heart. After a complete dissection of the heart and great vessels and their secondary branches, it was demonstrated that (1) no ductus arteriosus was present, (2) the aorta gave off only the right innominate and the left common carotid arteries, (3) the pulmonary artery gave rise to the left subclavian artery, and (4) the pulmonary artery, after giving origin to the right and left pulmonary arteries, was continued downward as the descending aorta.

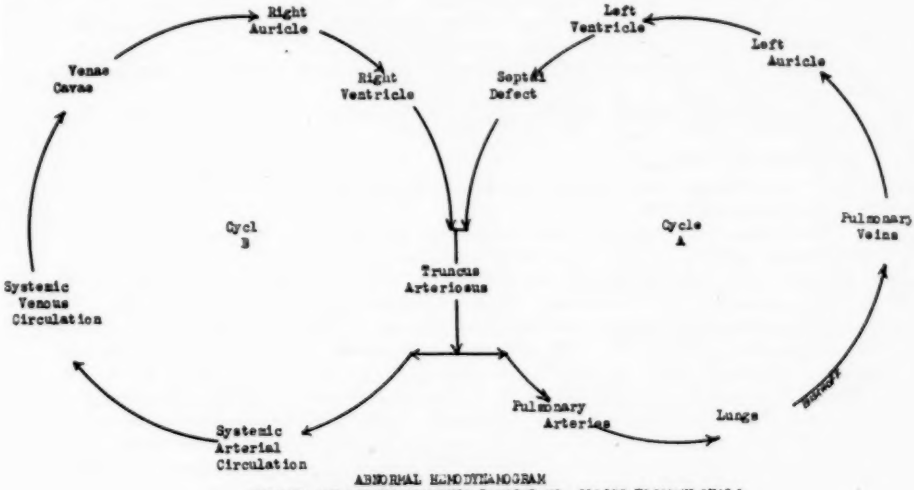


Fig. 2.

Upon opening the heart it was found that the tricuspid and mitral valves each had two leaflets. The leaflets of both valves were thickened along the free edges. There were small ball-like prominences which projected from the superior surface of the free edge of the posterior leaflet of the mitral valve. A large vessel overrode the septum, and the only communication between the left ventricle and this vessel was by way of an interventricular septal defect. This defect was ovoid in shape and measured 12 by 6 mm. in its greatest diameters. What appeared from the outside to be the pulmonary artery was actually a truncus arteriosus communis persistens. This vessel had four cusps, each of which was markedly thickened, fibrous, and red in color. A large vessel, unprotected by valves, was given off from the right side of the truncus so close to its origin that externally it had the appearance of a separate vessel with an individual origin from the base of the heart. This vessel divided into the right innominate and the left common carotid arteries approximately 1.5 cm. distal to its origin. The anterior and posterior coronary arteries originated near the base of the truncus. The truncus, after giving rise to the right and left pulmonary arteries, became the descending aorta. The left subclavian artery was given off from the truncus arteriosus by independent origin.

The remainder of the gross findings were within normal limits.

Microscopic examination of the tissues confirmed the gross impressions and also showed a generalized hemostasis as evidenced by a moderate red cell engorgement of all of the tissues of the thorax and abdomen and of the brain.

CASE 2.—R. M., aged 16 days, first began to have attacks of cyanosis at 6 days of age. These were associated with twitchings of the right side of the face and the right arm. These episodes occurred every two to three days until hospital entry at 16 days of age. The child was said never to have cried unless he was stimulated.

The past history revealed that the child was the product of the mother's third pregnancy. Two other siblings were living and well. The delivery was spontaneous and considered to have been normal.

Physical examination showed the child to be extremely cyanotic and dyspneic. The right side of the face twitched occasionally. The eyes, ears, and nose were normal. The lips were very blue. The lungs were clear to percussion and auscultation. The heart rate was rapid and the rhythm regular. There was a harsh systolic murmur at the third left interspace. The remainder of the physical examination was within normal limits.

The child convulsed continually. The convulsions appeared at more frequent intervals during feeding.

Throughout his hospital stay the child did poorly, and he died thirty hours after admission.

Post-Mortem Findings.—

At necropsy the lungs showed evidence of edema and congestion, as did the liver, pancreas, kidney, and brain.

The heart was moderately enlarged, weighing 32 Gm. as against a normal of 20 Gm. The tricuspid valve measured 3.4 cm. in circumference, and the mitral valve, 3.6 cm. in circumference. The right ventricular wall averaged 6.5 mm. in thickness, and the left ventricular wall averaged 6 mm. in thickness. The heart muscle was firm and of normal color. The endocardium showed no changes. The aorta and pulmonary artery were absent, being replaced by a single vessel. The valves of this common truncus had four semilunar cusps and measured 2.4 cm. in circumference. No branches were given off by the initial 6 cm. of the common truncus. The coronary arteries originated in a position corresponding to their openings in the aortic cone. They appeared slightly enlarged. The interauricular septum consisted of a thin endocardial membrane, which was perforated in numerous places. These defects measured from 1.0 to 8 mm. in diameter. The pars membranacea of the interventricular septum was defective. This defect measured 3 by 10 mm. and was so situated that blood from the left ventricle and right ventricle was injected directly into the common trunk. The ramifications of the common arterial trunk could not be followed since the latter had been severed at a point 6 cm. distal to the valve.

CASE 3.—C. S., aged 2 months, was admitted to The Children's Hospital on Dec. 14, 1942. The admission diagnosis was "probable" congenital heart disease. The chief complaint on admission was the appearance of cyanosis and wheezing respirations upon crying.

Physical examination revealed a pale, undernourished white male infant, who became very cyanotic when he began to cry. A marked dyspnea also appeared when the child cried. There was no obvious edema or clubbing. The eyes, ears, nose, and throat were normal. The lungs were considered to be within normal limits. The point of maximal impulse was not definitely visible or palpable, but seemed to be at the left anterior axillary line in the fourth and fifth interspaces. There was a soft systolic murmur best heard along the upper left sternal border (child crying). The rhythm was regular and the rate rapid. Examination of the abdomen was unsatisfactory because of the tense abdominal muscles (crying).

An electrocardiogram showed evidence of right ventricular strain.

X-ray examination of the chest revealed a massive collapse of the left lung with retraction of the heart and great vessels to that side.

Because of the massive collapse, bronchoscopy was performed. The right main bronchus was patent; however the left main bronchus was too narrow to admit the bronchoscope. The suction tip was used as a dilator. As the suction tip passed through the left main bronchus,

it gave the sensation of passing over a stricture. A follow-up film after bronchoscopy revealed the entire left lung to have undergone marked aeration.

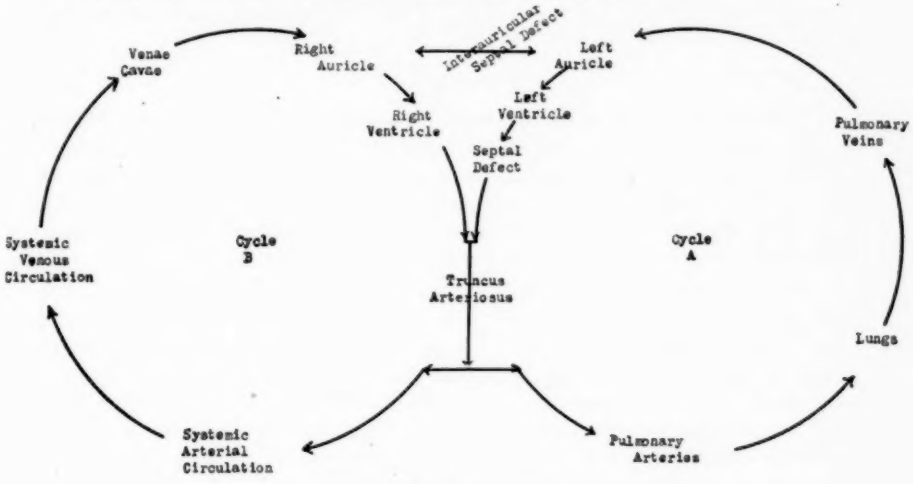
In spite of the apparent alleviation of the pulmonary condition, the child did poorly, became progressively more cyanotic, and expired on Feb. 16, 1942.

Post-Mortem Findings.—

The body was that of an emaciated but normally developed white male infant.

Permission to examine the brain was refused.

The thymus weighed 1.5 Gm. and was atrophic in appearance. No enlargement was noted of the bronchial and mediastinal lymph nodes. The trachea and bronchi were patent and grossly normal. Both lungs showed evidence of a pneumonic process. The middle third of the left lung was atelectatic due to compression by an enlarged heart.



ABNORMAL HEMODYNAMOGRAM
TRUNCUS ARTERIOSUS COMMUNIS PERSISTENS, CLOSED FORAMEN OVALE, ABSENT DUCTUS ARTERIOSUS, INTERVENTRICULAR SEPTAL DEFECT, INTERAURICULAR SEPTAL DEFECT. CASES R.M. AND C.S.

Fig. 3.

There were approximately 10 c.c. of clear, pale yellow fluid in the pericardial sac. The heart was rounded in shape and considerably enlarged. It weighed 59 Gm. against a normal of 27 Gm. for an infant 2 months old. Both ventricles were moderately dilated and showed marked hypertrophy of the ventricular musculature. The left ventricular wall averaged 10.5 mm. in thickness, and the right, 13.5 mm. The interventricular septum was defective at the base, the defect measuring 1.3 by 0.7 mm. The mitral valve measured 3.7 cm. in circumference, and the tricuspid valve, 4.1 cm. Those valves were not unusual in appearance except for a moderate thickening of the cusps, which did not appear to be on an inflammatory basis. Both auricles were moderately dilated but not hypertrophied. The interauricular septum showed a defect in its upper portion which measured 0.6 by 0.3 mm. This defect did not correspond to the anatomic position of the foramen ovale.

The aorta and pulmonary artery were replaced at their points of origin and to a length of 2.0 cm. by a common arterial trunk, which sat astride the interventricular defect and apparently received blood from both ventricles. The valve guarding the common trunk measured 3.8 cm. in circumference and possessed three cusps. The cusps were pink in color and larger and more fleshy than those ordinarily seen in the aortic or pulmonary valves. The nodules of Arantius were likewise distinctly larger than normal. The orifices of the right and left coronary arteries were slightly enlarged and were given off from the common trunk.

A vessel, unprotected by valves, was given off at a point 2 cm. above the origin of the common trunk, and this divided into the innominate, left common carotid, and left subclavian arteries. One centimeter beyond the origin of this vessel, the right and left pulmonary arteries were given off. Beyond this point the common truncus arched caudad and continued as the descending aorta.

Microscopic examination:

Lung: The vessels were intensely congested. The alveoli were crowded with leucocytes. Atelectasis was not prominent. One portion of the section showed beginning inflammatory changes; the alveolar spaces contained only a few red cells and polymorphonuclear leucocytes, but their walls were thickened due to leucocytic infiltration.

There was congestion of the remainder of the major visceral organs and granular degeneration of the kidney tubules.

DISCUSSION

It might be considered that with the only avenue of exit for blood from the left ventricle being by way of the interventricular septal defect, the right ventricle might be designated as a common ventricle. However since in all three of these cases the truncus overrode the septal defect, at each systole the blood from the left ventricle must have been forcibly injected into the common trunk with a minimum of mixing in the right ventricle.

In one of these children (Case 1), cyanosis was not a marked feature. This child had only the common trunk with no other complicating anomaly. In Case 2 there were, in addition to the common truncus, multiple perforations of the interauricular septum, which allowed for mixing of oxygenated and unoxygenated bloods prior to their injection into the common trunk. The third child, in addition to the common trunk, also had an interauricular septal defect and a compression of the air passage, which, according to the x-ray findings, undoubtedly interfered with aeration of the blood.

There is included a drawing of the heart (Fig. 1) of Case 1 opened through the right ventricle. This drawing has been labeled to demonstrate the major points.

We have also included two "hemodynamograms,"[2] which illustrate the blood circulation in the three cases. The first of these (Fig. 2) shows the circulation as it existed in Case 1. The second (Fig. 3) shows the circulation in Cases 2 and 3 and reveals the effect of introducing a shunt between the two auricles. These pictorial representations give an at-a-glance evaluation of the circulation as it existed during life. It may readily be seen that as the "back pressure" was increased in Cycle A, due to atelectasis, congestion, or edema, more blood was shunted to the systemic circulation. Thus less blood was offered for oxygenation to already poorly functioning organs (the lungs), with resulting anoxia, generalized engorgement of the brain and viscera, right heart failure, and death of the patient.

SUMMARY

1. Three cases of truncus arteriosus communis persistens are presented.

2. Hemodynamograms of the circulation as it existed in life are included, with remarks which speculate on the probable mechanism of death.

We are indebted to Dr. Carl Silverman for his permission to include his patient (Case 3) in this series.

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TRANSFUSIONS IN NEWBORN INFANTS THROUGH ABDOMINAL WALL SEGMENT OF UMBILICAL VEIN

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RECENT medical literature contains several articles dealing with transfusion of the newborn infant via the umbilical vein.[1, 2] The various techniques described have in common the employment of the umbilical vein *within* the umbilical cord. Their applicability is severely limited by the brief period during which the umbilical vein remains patent within the rapidly atrophying cord. Estimates of this period vary between twelve and forty-eight hours. Following is a preliminary report on a method which utilizes that portion of the umbilical vein which lies within the abdominal wall. Here the vein is readily available even after atrophy of the umbilical cord has occurred.

Technique.—A transverse cutaneous incision 2 cm. in engtth is made 1 cm. cephalad to the upper margin of abdominal insertion of the umbilical cord. Upon separation of the subcutaneous tissue, the umbilical vein is visualized as a whitish, longitudinal, tubular structure elevating the thin midline aponeurosis. A 0.5 cm. longitudinal incision through the aponeurosis is made on either side of the vein, and the latter is easily freed from the underlying transversalis fascia and peritoneum by blunt dissection with tissue forceps and grooved director. After loose application of a fine silk or catgut ligature around the upper exposed portion of the vein, a sharp-pointed scissors is employed to make a transverse nick through its anterior wall. A blunt-tipped nylon cannula, size 18 (or larger, if desirable), is then introduced cephalad until blood can be aspirated through it with ease. The ligature is then tied with a single hitch to effect snug approximation of the vein wall around the indwelling cannula, and transfusion is carried out. Upon termination of transfusion, the cannula is withdrawn, and the ligature is tightened and completed with a second hitch. Skin edges are approximated with two silk sutures.

Anatomical Considerations.—According to Arey,[3] the empty umbilical vessels contract and gradually lose their lumina by fibroblastic proliferation. This process extends through the first two or three months of postnatal life. Scam-

TABLE I. THE UMBILICAL VEIN AND DUCTUS VENOSUS IN THE NEWBORN INFANT (6 CASES)

PATH. NO.	AGE	LENGTH OF U.V. EXTRAPERITONEALLY	PATENT U.V.	DIAMETER U.V.	PATENT DUCTUS VENOSUS
32303	9 hr.	3.5 cm.	yes	0.4 cm.	yes
32842	15 hr.	2.5 cm.	yes	0.3 cm.	yes
32970	5 days	4.0 cm.	yes	0.3 cm.	yes
34333	5 hr.	2.5 cm.	yes	0.5 cm.	yes
35497	6 hr.	3.0 cm.	yes	0.4 cm.	yes
35498	3 days	3.0 cm.	yes	0.3 cm.	yes

This work was carried out in the Department of Pathology, the Bronx Hospital, New York, N. Y. Sincere thanks is given to Dr. Joseph Felsen, Director of Laboratories and Research, for his kind guidance and help.

mon and Norris,[4] in their review of 762 cases, report obliteration of the ductus venosus as follows: in 2.3 per cent the vessel is obliterated within the first week of life; in 18 per cent within the second week; in 37.5 per cent within the third week, and in 100 per cent, it is obliterated after the second month.

Table I is based on findings obtained from postmortem examination of six newborn full-term infants.

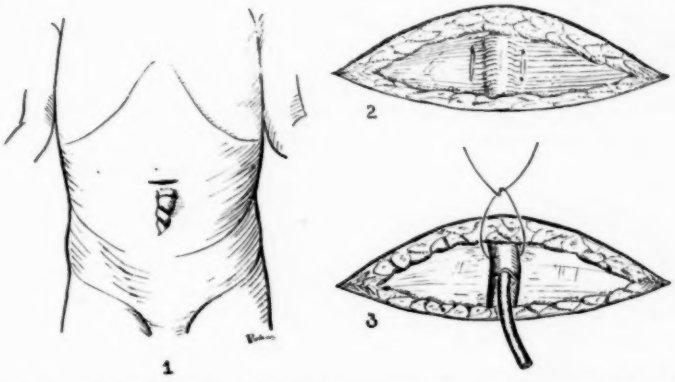

Fig. 1—Transabdominal wall approach to umbilical vein. *1*, Site of incision; *2*, close-up of cut-down site after separation of skin and subcutaneous tissue; *3*, umbilical vein isolated and cannula being introduced.

It is to be noted from Table I that the umbilical vein was found to be an extraperitoneal structure for a distance of 2.5 to 4.0 cm. cephalad to the upper margin of the umbilicus. Both the umbilical vein and the ductus venosus were patent in each case. The distance from the site of cut-down to the point of junction between the ductus venosus and the inferior vena cava varied between 6 and 8 cm.

Application.—To date, the above-described technique has been employed in transfusing one living newborn infant (Hospital Record No. 201217). This male, erythroblastotic infant, a spontaneous delivery at term, had replacement transfusion therapy instituted twenty-six hours after birth. All attempts at passing a cannula into the umbilical vein via the cord were unsuccessful. Thereupon, the transabdominal wall approach was made. Replacement transfusion, totalling 500 c.c. of blood withdrawn and 540 c.c. infused, was completed with ease.

CONCLUSIONS

A new approach to the umbilical vein is described. The length of time after birth during which this technique is applicable is as yet undetermined, but its usefulness far outlasts the approach via the cord. Moreover, the simplicity of technique, the large caliber of the umbilical vein, the toughness of

its wall, and its relative isolation from vital structures, render this site most desirable for transfusion techniques in the newborn infant.

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METHEMOGLOBINEMIA IN YOUNG INFANTS

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CLINICAL interest in cyanosis due to methemoglobinemia increased sharply with the introduction of sulfanilamide therapy and the early demonstration by Wendel[1] and Hartmann, Barnett, and Perley[2] that methylene blue was a very effective agent in its treatment or prevention. Wendel's work showed that methylene blue caused both formation and disappearance of methemoglobinemia and led to the following concept:

$$\text{Methylene Blue} + \text{Hemoglobin} \underset{97\%}{\overset{3\%}{\rightleftharpoons}} \text{methemoglobin} + \text{Leuko Methylene Blue}$$

$$\text{Leuko Methylene Blue} + O_2 \rightarrow \text{Methylene Blue}$$

In vivo, 97 per cent of the reaction was in the direction of methemoglobin → hemoglobin. Methylene blue was also found effective in the treatment of methemoglobinemia resulting from other known agents such as aniline shoe dyes and nitrates, and from unknown or "idiopathic" causes.[3] Although sulfanilamide is no longer a widely used drug or a frequent cause of methemoglobinemia, one of the newer sulfonamide derivatives, Promin† which is frequently used in conjunction with streptomycin in the treatment of tuberculosis, resembles sulfanilamide in its ability to produce methemoglobinemia and what at times may be confusing cyanosis.

While one of us (A. F. H.) was exploring, with some encouragement but no real success, the possibility that apparently idiopathic methemoglobinemia in the neonatal period might be due to low concentrations of normally occurring reducing substances in the tissues of such young infants, three different investigators, first Comly,[4] then Faucett and Miller,[5] and then Ferrant[6] showed that such infants might really be drinking well water containing nitrate and nitrite and developing cyanosis from such a cause. Recently our own experiences were confirmatory; i.e., instances of apparently "idiopathic" methemoglobinemia were really due to ingestion of well water contaminated with nitrate. There remained, however, the question as to why *only* the *young infants* and not other members of the family developed cyanosis. The following observations we believe answer the question.

EXPERIMENTAL OBSERVATIONS

A. Role of Nitrate.—That the nitrate ion when ingested and converted to nitrite can produce methemoglobinemia is not a new idea. In 1928, Barker and O'Hare[7] described a case of an adult male who, while receiving 15 Gm. per day

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†Sodium P,—P'—diaminodiphenylsulfone—N, N' didextrose sulfonate.

of ammonium nitrate, developed cyanosis "presumably because of methemoglobin." Eusterman and Keith[8] showed that a dosage of 12 Gm. per day of ammonium nitrate for two days produced methemoglobinemia in a 47-year-old woman. Roe[9] reports two fatal cases of methemoglobinemia in infants given bismuth subnitrate, and for many years it has been pediatric practice to treat diarrhea with bismuth subcarbonate rather than subnitrate to avoid the possibility of nitrite poisoning. Therefore, that the nitrite ion after reduction to nitrite is capable of producing methemoglobin in certain individuals is undoubtedly true.

It was first decided to determine whether the concentration of nitrate-ion fed infants was the important factor in their developing methemoglobinemia. The amount of ingested nitrate per kilogram of body weight per day as noted in the reported cases[4, 5, 6, 9] and in our own was found to vary from 37.1 mg. to 108.6 mg., with an average of 56.7 mg. per kilogram per day. In nitrite content, the well waters analyzed contained from a trace of 2 mg. per liter, amounts too small to produce methemoglobinemia.

An "artificial well water" was prepared which contained 1 mg. of nitrate ion per cubic centimeter, supplied in the form of sodium nitrate. The solution was autoclaved before incorporation into the infants' formula. Methemoglobin and total hemoglobin levels were determined by the method of Evelyn and Malloy.[10]

After feeding 50 mg. of nitrate ion per kilogram per day to four infants ranging in age from 11 days to 11 months for periods of two to eighteen days, the highest level of methemoglobin obtained was 0.75 Gm. per cent (5.3 per cent of the total hemoglobin). No cyanosis was evident. The dosage of nitrate ion was then doubled to 100 mg. per kilogram per day. The increased amount of nitrate was fed to four infants, 2 days to 6 months of age, for periods of six to nine days. The only noteworthy level of methemoglobin, 1.3 Gm. per cent (7.5 per cent of the total hemoglobin) was obtained in an infant 10 days of age eight days after the nitrate solution was added to his formula. Again, no cyanosis was evident.

Then 100 mg. of nitrate ion per kilogram per day were fed to infants who had previously been cyanotic due to the ingestion of well water containing nitrate and in whom treatment with methylene blue had been successful in relieving the cyanosis. The highest level in these babies, who were 6 and 7 weeks of age, was 11 per cent of the total hemoglobin, and this time cyanosis was apparent, but not marked.

Therefore, it appeared that there were other factors in addition to the quantity of nitrate ion ingested that determined whether or not an infant became cyanotic. We decided to investigate first such factors as bacterial well water contaminants and gastrointestinal flora with regard to nitrate reduction and then age, gastric acidity, and the level of intestinal absorption of nitrate.

B. Role of Gastrointestinal and Well Water Bacteria.—In the well waters described in the literature[4, 5, 6] and in the samples which we analyzed, bacterial contaminants were found. Ours were all of the so-called nonpathogenic varieties

and were chiefly *Aerobacter aerogenes*, aerophylic diplococci, and *Escherichia freundii*. All strains produced nitrite from nitrate.

The saliva, gastric juice, and stools of our cyanotic infants were cultured. Aerophilic streptococci and *A. aerogenes* were found in the saliva and gastric secretions of one infant. In another case, green streptococci, *Staphylococcus aureus*, and *Escherichia coli* were grown from the gastric juice, and a green streptococcus from the saliva. All of these organisms were then grown on simple peptone liquid media, one-half of which contained small amounts of sodium nitrate and one-half of which served as a control and contained no source of nitrate. In twenty-four to forty-eight hours, each tube containing the nitrate and one of the above organisms gave a strongly positive α-naphthalamine sulphonic acid test for nitrite. Therefore, all of the organisms found in the mouths and upper gastrointestinal tracts in two of our cyanotic babies were capable of reducing nitrate to nitrite.

In view of the above findings, some of the contaminated well water was fed to one of the previously cyanotic infants whose methemoglobin level was 0.1 Gm. per cent following therapy. After seventy-two hours, the methemoglobin level rose to 1.4 Gm. per cent or 12.1 per cent of the total hemoglobin, and the infant was cyanotic. Well water, after being sterilized by boiling for fifteen minutes, was fed to a two-month-old infant with meningitis and to another of the treated methemoglobinemia babies. The former's methemoglobin level did not exceed 0.2 Gm. per cent (2 per cent of the total hemoglobin) after sterile well water for two days, at which time the feedings had to be discontinued. The previously cyanotic infant developed methemoglobin levels of 1.26 Gm. per cent (11.1 per cent of the total hemoglobin) after six days and 1.0 Gm. per cent (9.5 per cent) after four days of sterile well-water feedings on two separate occasions. The infant who had been cyanotic continued to have positive gastric juice cultures for *A. aerogenes* and aerophilic streptococci while he was receiving the sterile well water.

In addition, three infants were fed sterilized well water plus interval feedings of a suspension of *A. aerogenes*. Two of the infants were prematures; each developed levels of 8.5 per cent methemoglobinemia in twenty-four hours, at which time the feedings were discontinued because one of the infants developed diarrhea. The third infant fed sterile well water and *A. aerogenes* had a strongly acid gastric juice and did not develop a noteworthy level of methemoglobin despite five days of nitrate feeding.

C. Role of Age and Gastric Acidity.—Examination of the gastric juice of the infants who developed appreciable levels of methemoglobinemia either on well water or nitrate water feedings revealed no free acid to be present and the pH to be greater than 4.0. All of the babies were less than 2 months of age.

In order to determine whether or not the gastric acidity had an effect on the survival of the nitrate reducing bacteria, the organisms which were cultured from the well water, saliva, gastric juice, and stools of one of our cyanotic infants were grown in culture media of various pH. All of the organisms including *A. aerogenes*, *Esch. freundii*, and *Esch. coli* grew in media of pH 5 to pH 7. None grew in media of pH 4.0. These findings are in keeping with

the observations made by Marriott, Hartmann, and Senn[11] on infants with diarrhea.

In addition, two of the previously cyanotic babies were placed on formulas containing lactic acid in addition to a source of nitrate. One infant, who had had a methemoglobin level of 0.75 Gm. per cent (7.6 per cent of the total hemoglobin), was placed on a lactic acid-well water formula. The methemaglobin level gradually fell over a period of three days to 0.13 Gm. per cent or 1.3 per cent of the total hemoglobin. The other infant, after attaining a level of 1.3 Gm. per cent of methemoglobin on a formula containing 100 mg. of nitrate ion per kilogram per day, was then treated with methylene blue intravenously and had a methemoglobin level of only 0.1 Gm. per cent after three days of a lactic acid-nitrate water formula.

D. Level of Absorption of Nitrate.—The organisms which we grew from the stools of two of our patients were *Esch. coli* and readily reduced nitrate to nitrite. Since these bacteria are present in almost all lower intestinal tracts, we postulated that the nitrate fed orally to normal babies was absorbed before coming into contact with organisms capable of converting nitrate to nitrite.

Subsequently we had an opportunity to verify this point in a 3-month-old infant in whom a transverse loop colostomy had been done shortly after birth. By injecting 200 mg. of nitrate ion into the colostomy, we obtained a level of methemoglobin of 2.6 Gm. per cent (25 per cent of the total hemoglobin) within four hours; the baby was markedly cyanotic. However, feeding the infant 600 mg. of nitrate ion daily for two days resulted in a methemoglobin level of only 0.5 Gm. per cent or 4 per cent of the total hemoglobin. Apparently most of the ingested nitrate had been absorbed before reaching the colon where the bacterial conversion to nitrite took place in this case.

DISCUSSION

From the foregoing observations we feel that only the young infants and not the older members of the family develop methemoglobinemia following the ingestion of well water containing nitrate, because of several factors. In young infants, nitrite-producing organisms can exist high in the gastrointestinal tract in sufficient numbers to reduce nitrate to nitrite before the former can be completely absorbed. This is because of the characteristic low acidity of the gastric juice in the neonatal period. It seems to us unlikely that the adult members of the family fail to develop methemoglobinemia merely because they ingest relatively less contaminated well water. In our group of control infants with good gastric acidity, very large amounts of nitrate were fed without the production of cyanosis or significant amounts of methemoglobinemia.

Many organisms, both pathogenic and nonpathogenic, are capable of converting nitrate to nitrite. No special significance need be attributed to the particular "nonpathogenic" contaminants grown from the well water other than that they were able to survive in the stomach and upper small intestine. However, we would predict that infants, in whom *Esch. coli* were permitted to infest heavily the stomach and duodenum by migrating from the lower intestinal tract

in the presence of a low gastric acidity, would also develop methemoglobinemia if fed nitrate water. Such a situation would simply be analogous to that described when nitrate was introduced into the transverse colon.

If severe cyanosis is present, treatment of choice is intravenous methylene blue, 1.0 to 2.0 mg. per kilogram.[1, 2] In prevention, while it is true that lactic acid added to the formula in the usual amounts (final concentrations 0.5 to 1 per cent) prevented the formation of methemoglobinemia, it seems safer to prohibit ingestion of nitrate water until infants are old enough to develop good gastric acidity.

SUMMARY AND CONCLUSIONS

1. The problem of methemoglobinemia in infancy following the ingestion of nitrate was studied.

2. Only infants who have a gastric juice pH higher than 4.0 and nitrate-reducing bacteria in the upper gastrointestinal tract develop methemoglobinemia from oral ingestion of water containing nitrate.

3. It was demonstrated that if nitrate is introduced into the colon, methemoglobinemia develops readily.

4. The treatment of choice for the cyanosis is intravenous administration of methylene blue, 1.0 to 2.0 mg. per kilogram.

5. The prevention of methemoglobinemia can be accomplished by adding lactic acid to the nitrate containing formula to inhibit bacterial growth in the upper gastrointestinal tract as well as by prohibiting the ingestion of nitrate.

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THE SIGNIFICANCE OF POSITIVE BLOOD CULTURES IN NEWBORN INFANTS

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IT IS not uncommon nursery experience to observe certain newborn infants who regularly lose weight beyond the usual expected time and who exhibit a lack of interest in nursing regardless of type of feeding. More often than not careful examination reveals no very convincing reason for the anorexia, listlessness, and accompanying weight loss. If allowed to go unchecked, loss of weight may be very considerable, and energetic and supportive treatment becomes imperative. The writers observed a suggested relationship between this clinical picture and blood cultures which were quite regularly positive for hemolytic staphylococci. In August, 1946, a study was begun for the purpose of clarifying this clinical impression.

This report is concerned with 323 blood culture samples taken from 240 infants, some of whom presented with surprising regularity the above clinical picture. In others the nursery course was uneventful. The number of blood cultures and the number of infants included in this study would seem to be significant.

In a partial review of the literature we find scant reference to bacteremia in the newborn infant. Older references to sepsis of the newborn infant are in most instances confusing and lacking in adequate blood studies. Usually these older reports described a severe type of illness, with death the usual rule, characterized by fever, severe gastrointestinal disturbance, jaundice, hemorrhage, and serious lesions noted at autopsy in the various body systems. The most informative study and the one most regularly referred to is that of Dunham.[1] She reported the findings in thirty-nine cases of septicemia of the newborn infant collected from the records of the New Haven Hospital and occurring over a period of five years. In thirty-four of her cases the diagnosis was made from blood cultures taken before death. She further recorded the findings in 115 blood cultures taken at random from forty-nine apparently healthy newborn infants. *Staphylococcus albus* was recovered in thirty-five instances from these apparently well infants. Dunham concluded that *Staph. albus*, since it could regularly be cultured from the skin of newborn infants, should not be considered as a cause of illness but rather as a skin contaminant when present in blood cultures in the neonatal period. This conclusion has been generally accepted as a fact.

The data recorded in this study suggest that hemolytic *Staph. albus* is capable of invading the blood stream of newborn infants with surprising regularity, and, if present in sufficient numbers, may cause regular and marked weight loss and at times serious signs of illness.

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All bacteriologic studies were done under the direction of Dr. William E. Bray, director of clinical laboratories at the University of Virginia Hospital. The helpful cooperation of this department, so essential to this investigation, is gratefully acknowledged.

The procedure employed in obtaining blood samples was as follows: The skin was cleansed with iodine and alcohol. Blood was obtained from the internal jugular vein. In a few instances the femoral vein was used. Blood samples were placed in dextrose carbonate hormone media and in blood agar at forty-eight hours and ninety-six hours. Throughout most of the study subcultures were made on Löffler's medium and plain agar. Toward the end of the study subcultures were made in dextrose lactose and mannite media.

Table I describes the relative frequency of blood cultures positive for hemolytic staphylococci in thirty-four infants from whom blood samples were taken for cause. In every instance the cause was progressive loss of weight frequently associated with anorexia, lassitude, or irritability, for which signs of illness no obvious reason was apparent. All thirty-four infants were observed toward the end of this study and the identity of the organisms seemed clearly established.

Hemolytic *Staph. albus* was identified from culture in twenty-one instances; nonhemolytic *Staph. albus* was cultured in three instances; hemolytic *Staphylococcus aureus* in four instances; nonhemolytic *Staph. aureus* in one instance. Other organisms recovered and considered as contaminants were diphtheroids in one instance, *Bacillus subtilis* in one instance. First cultures were taken at from seven to sixteen days of age, the average age for first culture being ten days. First cultures were positive for hemolytic staphylococci, usually of the albus variety, in 64.7 per cent of this series. Granted that *Staph. albus* is a very common contaminant of blood cultures, it is difficult to suppose that contamination from the skin would occur with such frequency and regularity.

As a control series blood culture samples were taken at random from fifty newborn infants. No infant was considered eligible for this control series whose progress in the nursery was unsatisfactory, or who showed any signs of illness. Blood samples were taken at different seasons of the year. The identity of the organisms recovered from positive cultures seemed clearly established. Hemolytic *Staph. albus* was identified in thirteen instances; nonhemolytic *Staph. albus* in three instances; hemolytic *Staph. aureus* in four instances. Other organisms recovered and considered as contaminants were diphtheroids in one instance, hay bacillus in one instance.

As a second control series it seems permissible to include blood samples from fifty-six additional newborn infants. These infants were observed early in the study when one technician had difficulty in distinguishing between *Staph. albus* and *Staph. aureus*. For this reason the staphylococci recovered in cultures will be referred to as hemolytic and nonhemolytic staphylococci. In thirty positive cultures hemolytic staphylococci were identified in twenty-one instances, nonhemolytic staphylococci in one instance. Other organisms recovered and considered as contaminants were *Bacillus aerogenes* (1), coliform bacillus (1) beta

TABLE I

NO.	HISTORY NUMBER	NURSERY	FIRST CULTURE			SECOND CULTURE		THIRD CULTURE		FOURTH CULTURE	
			DATE	AGE IN DAYS	RESULT	DATE	RESULT	DATE	RESULT	DATE	RESULT
1	237437	WCN	26 March 47	12	*Staph. albus*, hemolytic	10 April 47	Negative				
2	238173	PCN	17 April 47	16	*Staph. albus*, hemolytic						
3	238219	PCN	17 April 47	14	*Staph. albus*, hemolytic; micrococci						
4	238280	WCN	13 April 47	9	Negative						
5	238507	WCN	16 April 47	7	*Staph. albus*, hemolytic						
6	238758	WCN	26 April 47	11	Negative						
7	238823	WCN	26 April 47	9	Negative						
8	238843	WCN	29 April 47	11	*Staph. albus*, hemolytic	3 May 47	*Staph. aureus*, hemolytic	9 May 47	Negative		
9	239533	WCN	18 May 47	10	*Staph. albus*, nonhemolytic						
10	239559	WCN	18 May 47	10	*Staph. albus*, hemolytic	22 May 47	Negative				
11	240235	WCN	5 June 47	10	*Staph. albus*, hemolytic	11 June 47	Negative				
12	240297	WCN	7 June 47	11	*Staph. aureus*, hemolytic	11 June 47	Negative				
13	240329	WCN	5 June 47	8	Negative						
14	240387	WCN	7 June 47	9	*Staph. albus*, hemolytic	11 June 47	Negative				
15	240388	WCN	8 June 47	10	Negative						
16	240529	WCN	12 June 47	9	*Staph. albus*, hemolytic	17 June 47	Negative				

17	240994	WCN	25	June	47	11	*Staph. albus*, hemolytic; *Staph. aureus*, hemolytic and nonhemolytic	30	June	47	*Staph. aureus*, nonhemolytic	6	July	47	*Staph. albus*, hemolytic	11	July	47	Negative
18	241054	WCN	25	June	47	10	Negative												
19	241398	WCN	3	July	47	9	Diphtheroids												
20	241541	WCN	9	July	47	11	*Staph. albus*, hemolytic	12	July	47	*Bacillus subtilis*	6	Aug.	47	Negative				
21	242108	WCN	22	July	47	9	*Staph. albus*, hemolytic	28	July	47	*Staph. albus*, hemolytic; *Staph. aureus*, hemolytic	4	Aug.	47	Negative				
22	243030	CCN	13	Aug.	47	9	*Staph. albus*, hemolytic	18	Aug.	47	*Staph. albus*, hemolytic	20	Aug.	47	*Staph. albus* hemolytic				
23	245174	WCN	6	Oct.	47	10	*Staph. albus*, hemolytic												
24	245734	WCN	23	Oct.	47	11	*Staph. albus*, hemolytic	31	Oct.	47	*Staph. albus*, hemolytic								
25	245813	WCN	26	Oct.	47	13	*Staph. albus*, hemolytic	2	Nov.	47									
26	245947	PCN	24	Oct.	47	7	*Staph. albus*, hemolytic	3	Nov.	47	Negative								
27	246623	WCN	11	Nov.	47	7	Negative												
28	246994	WCN	22	Nov.	47	9	Negative												
29	247487	PCN	8	Dec.	47	10	Diphtheroids												
30	247635	WCN	14	Dec.	47	12	*Staph. albus*, hemolytic	19	Dec.	47	*Staph. albus*, hemolytic								
31	247762	WCN	13	Dec.	47	8	*Staph. aureus*, hemolytic	18	Dec.	47	*Staph. albus*, hemolytic	23	Dec.	47	Negative	26	Dec.	47	*Staph. albus*, nonhemolytic
32	247874	WCN	19	Dec.	47	11	Negative												
33	248320	WCN	30	Dec.	47	9	Negative												
34	249080	WCN	20	Jan.	48	9	*Staph. albus*, hemolytic												

WCN, White Children's Nursery.
PCN, Premature Children's Nursery.
CCN, Colored Children's Nursery.

TABLE 11

NO.	HISTORY NUMBER	NURSERY	FIRST CULTURE			SECOND CULTURE			THIRD CULTURE			FOURTH CULTURE		
			DATE	AGE IN DAYS	RESULT	DATE	AGE IN DAYS	RESULT	DATE	AGE IN DAYS	RESULT	DATE	AGE IN DAYS	RESULT
1*	216707	PCN	30 Aug.	15	Hemolytic staphylococcus	31 Aug.	45	Negative	3 Sept.	45	Hemolytic staphylococcus	3 Sept.	45	Hemolytic staphylococcus
2*	218099	WCN	5 Oct.	11	Hemolytic staphylococcus	7 Oct.	45	Negative	7 Oct.	45	Negative	10 Oct.	45	Hemolytic staphylococcus
3	218209	WCN	7 Oct.	10	Diphtheroids	13 Oct.	45	Hemolytic staphylococcus	15 Oct.	45	Hemolytic staphylococcus	25 Oct.	45	Negative
4	218361	WCN	13 Oct.	11	Hemolytic staphylococcus	18 Oct.	45	Hemolytic staphylococcus	25 Oct.	45	Negative			
5*	219846	WCN	23 Nov.	9	Hemolytic staphylococcus	27 Nov.	45	*Str. fecalis;* hemolytic staphylococcus	1 Dec.	45	Negative	1 Dec.	45	Hemolytic staphylococcus
6	220648	WCN	18 Dec.	12	Hemolytic staphylococcus	20 Dec.	45	Hemolytic staphylococcus	28 Dec.	45	Negative			
7	226034	WCN	25 May	11	Hemolytic staphylococcus	27 May	46	Hemolytic staphylococcus	1 June	46	Hemolytic staphylococcus	3 June	46	Negative
8	226120	WCN	31 May	15	Hemolytic staphylococcus	3 June	46	Hemolytic staphylococcus	7 June	46	Hemolytic staphylococcus			
9*	226644	WCN	8 June	9	Nonhemolytic staphylococcus	12 June	46	Nonhemolytic staphylococcus	15 June	46	Negative	22 June	46	Diphtheroids
10	229517	WCN	26 Aug.	10	Negative	27 Aug.	46	Nonhemolytic staphylococcus	5 Sept.	46	Hemolytic staphylococcus	12 Sept.	46	Diphtheroids
11	229562	WCN	25 Aug.	7	Hemolytic staphylococcus	27 Aug.	46	Hemolytic staphylococcus	1 Sept.	46	Hemolytic staphylococcus	4 Sept.	46	Flavobacterium
12	230226	PCN	24 Sept.	18	Nonhemolytic staphylococcus	29 Sept.	46	Hemolytic staphylococcus	4 Oct.	46	Negative			

13*	230228	PCN	14	Sept.	46	9	Negative	15	Sept.	46	Hemolytic staphylococcus	24	Sept.	46	Diphtheroids	29	Sept.	46	Beta hemolytic streptococcus Hemolytic staphylococcus
14	230783	WCN	24	Sept.	46	6	Hemolytic staphylococcus	27	Sept.	46	Hemolytic staphylococcus	29	Sept.	46	Negative	7	Oct.	46	Negative
15	232293	WCN	8	Nov.	46	10	Nonhemolytic staphylococcus	10	Nov.	46	Nonhemolytic staphylococcus	16	Nov.	46	Hemolytic staphylococcus				
16	235349	PCN	28	Jan.	47	11	Hemolytic staphylococcus	2	Feb.	47	*B. coli*	6	Feb.	47	Nonhemolytic staphylococcus	9	Feb.	47	Negative
17	238843	WCN	29	April	47	11	Hemolytic staphylococcus	3	May	47	Hemolytic staphylococcus	9	May	47	Negative				
18	240994	WCN	25	June	47	11	Hemolytic and nonhemolytic staphylococcus	30	June	47	Nonhemolytic staphylococcus	6	July	47	Hemolytic staphylococcus	11	July	47	Negative
19	242108	WCN	22	July	47	9	Hemolytic staphylococcus	28	July	47	Hemolytic staphylococcus	4	Aug.	47	Negative				
20	243030	CCN	13	Aug.	47	9	Hemolytic staphylococcus	18	Aug.	47	Hemolytic staphylococcus	20	Aug.	47	Hemolytic staphylococcus				
21	245734	WCN	23	Oct.	47	11	Hemolytic staphylococcus	31	Oct.	47	Hemolytic staphylococcus								
22	247635	WCN	4	Dec.	47	12	Hemolytic staphylococcus	19	Dec.	47	Hemolytic staphylococcus								
23	247762	WCN	13	Dec.	47	8	Hemolytic staphylococcus	18	Dec.	47	Hemolytic staphylococcus	23	Dec.	47	Negative	26	Dec.	47	Nonhemolytic staphylococcus

			FIFTH CULTURE				SIXTH CULTURE				SEVENTH CULTURE			
1			10	Sept.	45	B. proteus	12	Sept.	45	Negative	21	Sept.	45	Negative
2			21	Oct.	45	Negative								
5			12	Dec.	45	Hemolytic staphylococcus								
9			26	June	46	Negative								
13			3	Oct.	46	Negative								

hemolytic streptococcus (1) diphtheroids (2) and micrococci (1). The percentage of cultures positive for staphylococci in the combined control series was 39.56 per cent.

Table II describes the regularity with which repeat cultures positive for hemolytic staphylococci were obtained in twenty-three infants from which blood samples were taken for cause and found to be positive for hemolytic staphylococci.

Repeat cultures were positive for staphylococci in every instance, or 100 per cent. It would seem unreasonable to believe that staphylococci present in the skin surface could contaminate blood cultures with this regularity even if no cleansing of the skin surface had been practiced. The frequency with which repeat positive cultures were obtained compares favorably with repeat positive cultures in bacteremia in other age groups and of more familiar etiology.

From Jan. 2, 1947, to Jan. 31, 1947, 200 blood cultures were drawn at the University of Virginia Hospital on all services. The findings in these two hundred consecutive blood cultures were as indicated in Table III.

TABLE III

Adults: total cultures, 148; positive, 25; negative, 123.	
Hemolytic staphylococci	6
Nonhemolytic staphylococci	5
Diphtheroids	7
Micrococci	4
Yeastlike organisms	1
Mold	2
Total	25
Children: total cultures, 11; positive, 2; negative, 9.	
Hemolytic staphylococci	1
Mold	1
Total	2
Newborn infants: total cultures, 41; positive, 22; negative, 19.	
Hemolytic staphylococci	14
Hemolytic staphylococci and Beta hemolytic streptococci	1
Nonhemolytic staphylococci and micrococci	1
Diphtheroids	2
Micrococci	2
Coliform bacilli	1
Bacillis pyocyaneus	1
Total	22

	TOTAL CULTURES	TOTAL POSITIVE	POSITIVE FOR STAPH.	PER CENT POSITIVE	PER CENT POSITIVE FOR STAPH.
Adults	148	25	11	16.88	7.44
Children	11	2	1	18.18	9.09
Newborn infants	41	22	16	53.65	39.02
Total	200	49	28	24.50	14.00

For the purpose of further investigating the probability of contamination from the skin, the following observations were made with forty newborn infants as subjects. The skin of the lateral side of the neck was prepared with iodine and alcohol in the usual fashion: 5 c.c. of reconstituted dried plasma were drawn into a syringe, both syringe and needle having previously been autoclaved; 2.5 c.c. of the plasma were placed in beef broth and cultured, thus serving as con-

trols. The 2.5 c.c. of plasma remaining in each syringe were injected under the skin in the posterior triangle of the neck behind the posterior border of the belly of the sternomastoid muscle at the juncture of the lower and middle thirds of the muscle. The needle was inserted in the same direction and manner as was regularly done in obtaining blood samples for culture. Plasma was injected and aspirated back and forth several times and was placed in separate flasks of broth for culture. In the final aspiration at least 1.5 c.c. of injected plasma were recovered. This would seem an ample amount to insure thorough rinsing of the lumen of the needle. In one instance both control and injected cultures were positive for *Staph. albus*. We assume that the syringe was contaminated in this one instance and these two cultures were discarded. In the remaining thirty-nine instances the control cultures showed no growth. Of the thirty-nine culture flasks containing samples of injected plasma, ten showed bacterial growth. The organisms were identified as hemolytic *Staph. albus* in eight instances, colon bacillis in one instance, and hemolytic *Staph. aureus*, coagulase positive, in one instance.

As a control study the above procedure was repeated in twenty older infants and runabout children. Samples of injected plasma and controls were negative with one exception. In one instance only a sample of injected plasma was positive for hemolytic *Staph. aureus*.

It would seem to be clearly established that the bacterial flora of the skin of newborn infants is unusually rich in members of the staphylococcus group as compared with the skin of other age groups.

It is a routine nursery procedure in our hospital to apply penicillin ointment once a day to the skins of all newborn infants. This procedure has proved very effective in the prevention of impetigo neonatorum. No studies have been made to determine the possible effect of this daily procedure on the instance of positive blood culture.

If hemolytic *Staph. albus* invades the blood stream of newborn infants with and without symptoms as suggested in this study, it would seem not unlikely that such bacteremia might be prevented.

Preventive therapy was attempted in three separate series of infants. The plan of study was as follows: Beginning at 24 hours of age, every other full-term infant admitted to our nursery was given 5,000 units of penicillin every three hours for a period of four days. Twenty-four hours after the last dose of penicillin a blood sample was drawn. Those infants not receiving penicillin were used as controls.

Series I consisted of eighteen treated infants and eighteen controls. Series II consisted of twenty-five treated infants and twenty-four controls. Series III consisted of twenty-four treated infants and twenty-five controls. From the sixty-seven treated patients twenty cultures positive for staphylococci were obtained. From the sixty-seven controls twenty cultures positive for staphylococci were obtained. Penicillin therapy started at the end of twenty-four hours and administered in the above doses was not effective in the prevention of cultures positive for staphylococci. Perhaps better results might be expected if prevention treatment were delayed until the fourth or fifth day. The rapid

turnover in our nurseries during the past year has prevented further study along these lines.

TREATMENT

Penicillin has been regularly used in the treatment of the clinical picture described in this report. In some instances the addition of sulfadiazine has appeared to speed recovery. Ten thousand units of penicillin intramuscularly every three hours is the dosage presently used. With this dosage, prompt and regular weight gains have been the rule with corresponding improvement in the infant's general condition. Early diagnosis and prompt therapy have markedly reduced the necessity for parental infusions and blood transfusions.

Figs. 1 to 8 present graphically the nursery course in regard to weight curve type of therapy and response to therapy in typical examples.

Additional case protocols are included which describe response to therapy and the frequency of repeat positive cultures.

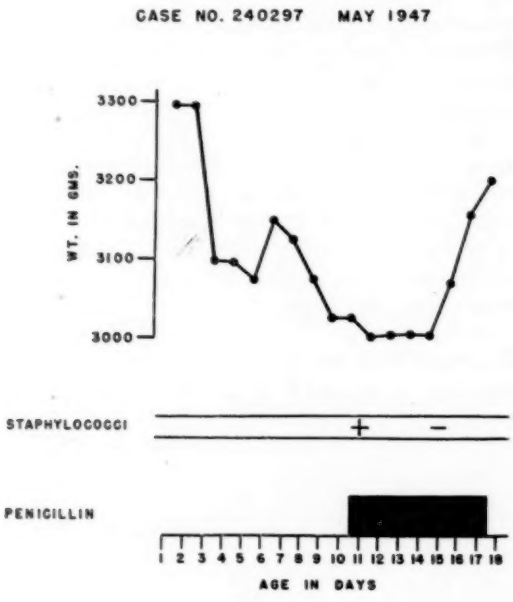

Fig. 1.

CASE PROTOCOLS

CASE 217163.—A white female infant was born Aug. 29, 1945, weighing 2,890 Gm. Delivery followed a normal pregnancy and labor. The nursery course was uncomplicated until the ninth day when the infant began to lose weight. Four days later she began vomiting and developed a watery diarrhea. This was treated in the usual manner, and subsided by the twenty-second day. However, the patient still failed to gain weight and ran an elevation of temperature from the twenty-fourth to the thirtieth day. A blood culture drawn on the thirty-second day was reported as positive for hemolytic staphylococci. A blood culture

repeated two days later was again positive for hemolytic staphylococci. The infant was treated with penicillin 5,000 units q3h and sulfadiazine .065 Gm. five times daily. With this therapy a satisfactory weight curve was established. After two negative blood cultures were obtained the child was discharged in good condition on the fifty-ninth hospital day. No follow-up was available.

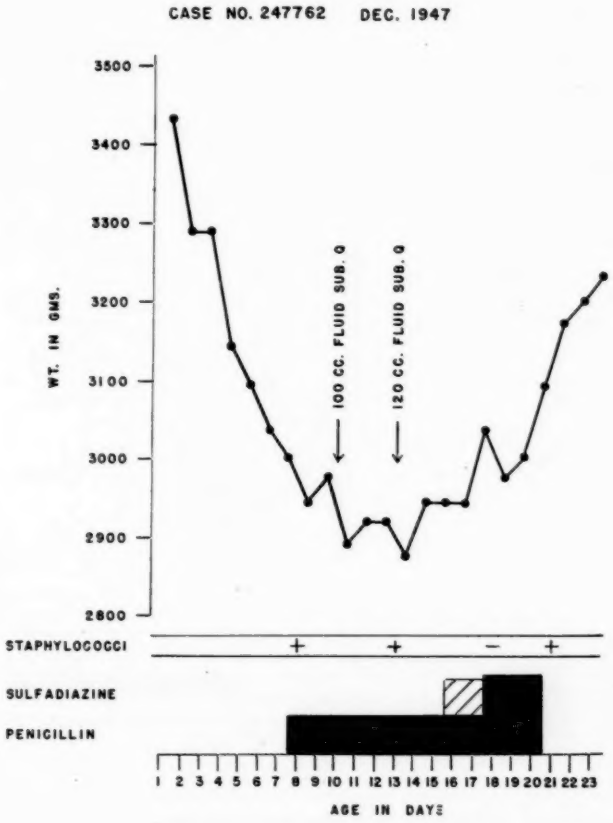

Fig. 2.

CASE 218209.—A white male infant was born Sept. 28, 1945, weighing 3,775 Gm. Delivery followed a normal pregnancy and labor. This infant was apparently well and had a good appetite, but failed to make satisfactory weight gain. A blood culture obtained on the tenth day was reported positive for diphtheroids. A repeat culture on the sixteenth day was reported as positive for hemolytic staphylococci. Two blood cultures were obtained on the eighteenth day and sent to separate laboratories. They were both reported as positive for hemolytic staphylococci. Penicillin 5,000 units q3h, sulfadiazine .065 Gm. six times daily were administered with a satisfactory weight gain being established promptly. He was discharged on the thirty-second day in good condition following a negative blood culture. He was seen three weeks after discharge and was in good condition.

Fig. 3.

CASE 218361.—A white male infant was born Oct. 3, 1945, weighing 2,835 Gm. Delivery followed a normal pregnancy and labor. The nursery course was complicated by anorexia and failure to gain weight. There were no temperature elevations and physical examination was negative. Blood culture drawn on the eleventh day was reported positive for hemolytic staphylococci. A repeat blood culture on the sixteenth day was again positive for this organism. Penicillin 5,000 units and sulfadiazine .065 Gm. five times daily were started on the seventeenth day. The infant's appetite improved immediately and he began making daily weight gains. He was discharged on the thirty-second day in good condition following a negative blood culture. No follow-up was available. (See Fig. 3.)

CASE 218809.—A white female infant was born Oct. 17, 1945, weighing 3,675 Gm. Delivery followed a normal pregnancy and labor. The nursery course was complicated by anorexia and a steady weight loss. A blood culture drawn on the eleventh day was reported as positive for hemolytic staphylococci. A repeat blood culture on the thirteenth day was

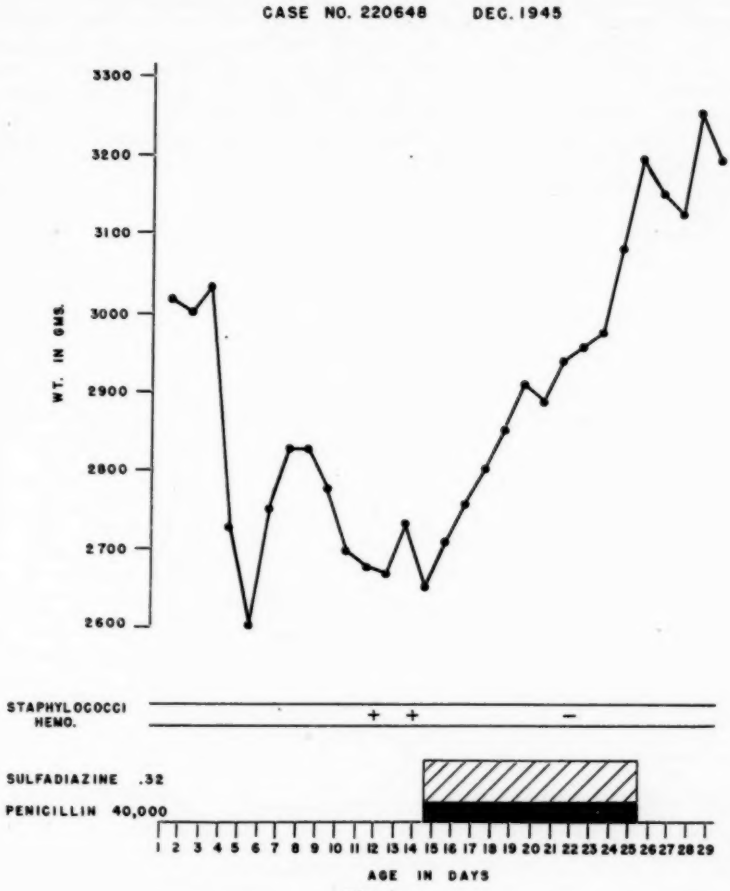

Fig. 4.

lost. On the thirteenth day the patient was started on penicillin 5,000 units q3h. A satisfactory weight curve was established. He was discharged on the twenty-second day in good condition following a negative blood culture. No follow-up was available.

CASE 220648.—A white male infant was born Dec. 7, 1945, weighing 3,015 Gm. Delivery followed a normal pregnancy and labor. The nursery course was complicated by anorexia and a steady weight loss. At no time was there an elevation of temperature and the physical examination was negative. A blood culture drawn on the twelfth day was reported positive for hemolytic staphylococci. A repeat blood culture on the fourteenth day was positive for the same organism. Penicillin 5,000 units q3h and sulfadiazine .065 Gm. five times daily were started on the fifteenth day. There was an immediate improvement in appetite and a satisfactory weight gain was established. The infant was discharged in good condition on the twenty-ninth hospital day following a negative blood culture. No follow-up was available. (See Fig. 4.)

CASE 219846.—A white male infant was born Nov. 10, 1945, weighing 3,600 Gm. Delivery followed a normal pregnancy and labor. The nursery course was complicated by anorexia and inconsistent weight gain. Sulfadiazine .065 Gm. five times daily was started. A blood culture drawn on the eleventh day was reported as positive for penicillin resistant strain of hemolytic staphylococci. Penicillin 10,000 q3h intramuscularly was given in addition to the sulfadiazine. A blood culture drawn on the fifteenth day was positive for hemolytic staphylococci, again penicillin resistant, and *Streptococcus fecalis*. The infant's appetite picked up and he gained weight consistently. Blood culture on the eighteenth day was negative. Therapy was discontinued on the twenty-fourth day. A blood culture was drawn on the twenty-eighth day and he was discharged on that day in good condition. This last blood culture was reported as positive for hemolytic staphylococci.

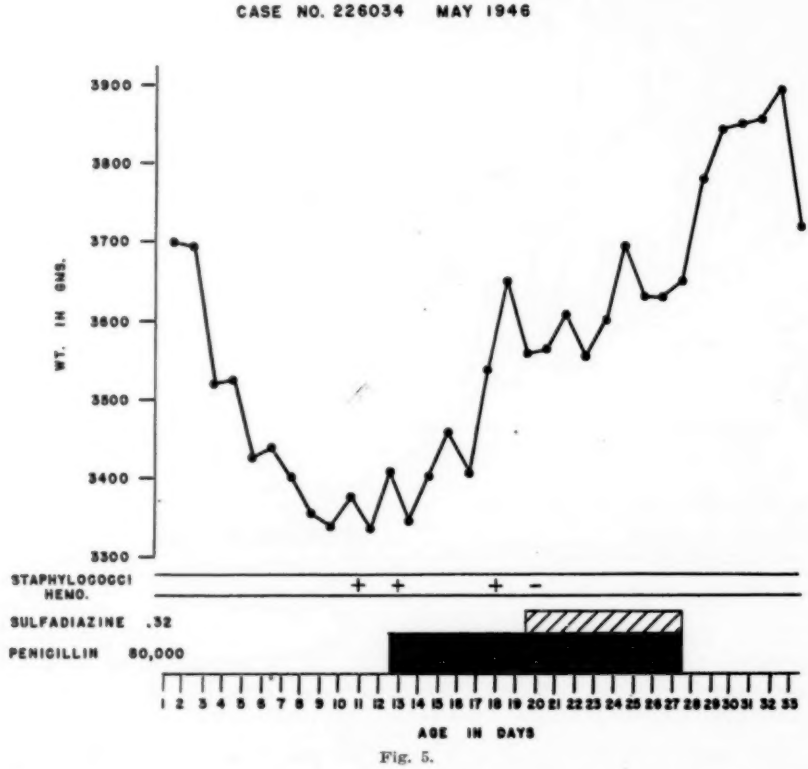

Fig. 5.

CASE 230783.—A white male infant was born Sept. 19, 1946, weighing 3,310 Gm. Labor was complicated by slight premature separation of placenta near term. Weight gains were unsatisfactory and a blood culture drawn on the sixth hospital day was positive for hemolytic staphylococci. A second blood culture drawn on the ninth hospital day was again positive for hemolytic staphylococci. Penicillin 10,000 units q3h was started on the tenth hospital day. A blood culture drawn on the eleventh hospital day was negative; however, weight gains were not satisfactory until the sixteenth hospital day. A final blood culture drawn on the nineteenth hospital day was negative and the infant was discharged on the twenty-first day after six days of progressive weight gain. The child has been followed in the clinic and is a healthy infant.

CASE 226034.—A white female infant was born May 15, 1946, weighing 3,700 Gm. The mother had active tuberculosis and a low cervical cesarean section was performed. There were only three weight gains in the first eleven days. A blood culture drawn on the eleventh day was reported as positive for hemolytic staphylococci. Penicillin 10,000 units q3h were started on the thirteenth hospital day. Following this therapy weight gains were satisfactory. Blood cultures drawn on the thirteenth and seventeenth hospital days were again reported as positive for hemolytic staphylococci. Sulfadiazine .065 Gm. q4h five times daily was started on the nineteenth hospital day. A blood culture drawn on the twentieth hospital day was reported as negative. The infant was discharged on the thirty-second hospital day. No follow-up was available. (See Fig. 5.)

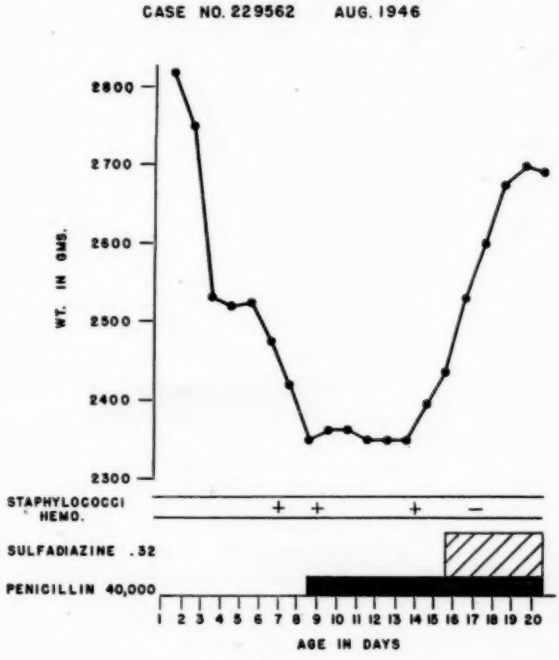

Fig. 6.

CASE 233835.—A white female infant was born Dec. 8, 1946, weighing 3,180 Gm. Delivery followed a normal pregnancy and labor. There were no weight gains for the first seven days. Penicillin 10,000 units q3h was started. A blood culture was not taken until the following day. However, it was positive for hemolytic staphylococci. The weight gains were satisfactory following instigation of penicillin. This therapy was discontinued on the fourteenth day. The infant was discharged on the fifteenth day following a negative blood culture. Follow-up revealed a well baby.

CASE 227302.—A white male infant was born June 19, 1946, weighing 3,490 Gm. Delivery followed a normal pregnancy and labor. Weight gains were unsatisfactory the first eleven days. A blood culture drawn on the eleventh day was reported as positive for hemolytic staphylococci. Penicillin 5,000 units q3h was started. Following this therapy weight gains were satisfactory. A blood culture drawn on the thirteenth hospital day was reported as negative. The infant was discharged on the eighteenth hospital day.

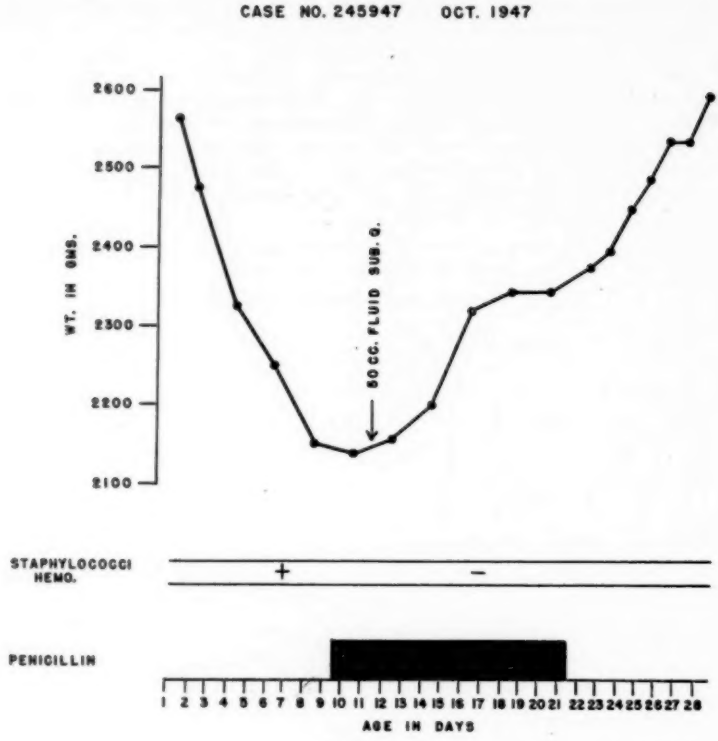

Fig. 7.

CASE 232178.—A female Negro infant was born Oct. 27, 1946, weighing 2,310 Gm. Delivery followed a normal pregnancy and labor. Weight loss was progressive for the first twelve days. A blood culture drawn on the tenth day was positive for hemolytic staphylococci. Penicillin 10,000 units intramuscularly q3h was started on the twelfth day. Weight gains were progressive following instigation of this therapy. She was discharged on the thirtieth day following a negative blood culture. Follow-up revealed a well baby.

CASE 232076.—A white male infant was born Oct. 24, 1946, weighing 1,956 Gm. Pregnancy was complicated by a premature onset of labor. Nursery course was complicated by anorexia and failure to gain weight. A blood culture drawn on the nineteenth day was positive for hemolytic staphylococci. Penicillin 10,000 units intramuscularly q3h was started on the twenty-second day and continued for seven days. Weight gains were progressive following instigation of this therapy. He was discharged on the fortieth day following a negative blood culture.

CASE 232230.—A white female infant was born Oct. 28, 1946, weighing 2,820 Gm. Pregnancy was complicated by pre-eclampsia and questionable active tuberculosis. Weight gains were unsatisfactory in spite of good appetite. A blood culture drawn on the ninth day was positive for micrococci. A second culture was drawn on the thirteenth day and penicillin 10,000 units q3h intramuscularly was started. The infant's gains improved and penicillin was discontinued on the nineteenth day. The second blood culture was lost. A

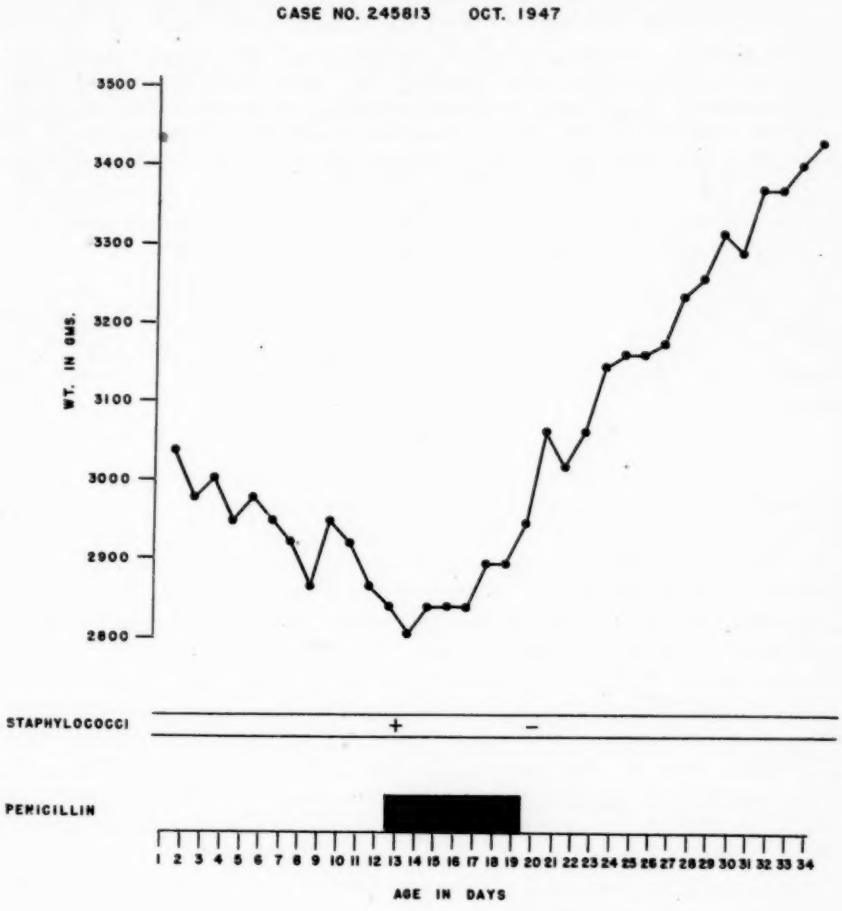

Fig. 8.

third culture drawn on the twentieth day was reported as positive for hemolytic staphylococci. Penicillin 10,000 units q3h was again started. The infant was discharged on the twenty-ninth day following a negative blood culture.

Case 232293.—A white female infant was born Oct. 30, 1946, weighing 3,650 Gm. Delivery followed a normal pregnancy and labor. On the fifth day she began regurgitating several feedings daily. On the eighth day she began losing weight daily. A blood culture was drawn on the eighth day and reported as positive for hemolytic staphylococci. Penicillin 10,000 units intramuscularly q3h was started on the twelfth day. A second blood culture was drawn on the twelfth day and was again positive for hemolytic staphylococci. Penicillin was discontinued on the seventeenth day, at which time another blood culture was obtained. The infant was discharged on the eighteenth day after five days of progressive weight gains. The third culture was reported as positive for hemolytic staphylo-

cocci. The infant returned to the clinic in two weeks having gained fourteen ounces. A blood culture taken at that time was negative.

CASE 229562.—A white female infant was born Aug. 19, 1946, weighing 2,815 Gm. Delivery followed a normal pregnancy and labor. The infant made only two small weight gains in the first thirteen days. Blood culture drawn on the seventh day was positive for hemolytic staphylococci. Penicillin 5,000 units intramuscularly q3h was started on the ninth day. Blood cultures drawn on the eleventh and fourteenth days were positive for hemolytic staphylococci. Sulfadiazine .065 Gm. q4h was started on the sixteenth day. Penicillin and sulfadiazine were discontinued on the twentieth day, at which time the infant was discharged. Discharge followed six days of progressive weight gains and a negative blood culture. Follow-ups have revealed a healthy child. (See Fig. 6.)

One death occurred in this study. Blood culture was positive for hemolytic staphylococci and peritonitis was thought to be present. At operation eighteen inches of bowel was found to be gangrenous with numerous perforations. In certain other infants signs of illness were of sufficient severity as to cause real concern.

COMMENT

It would seem to be clearly established that the bacterial flora of the skin of newborn infants is unusually rich with members of the staphylococcus group of bacteria as compared to the skin in other age groups. The interpretation of the data described in this report must of necessity be tempered by this fact. It is difficult to believe that the high incidence of positive blood cultures taken for cause and the frequency of positive repeat cultures can be explained solely by contamination from the skin.

Despite the fact that contamination of blood cultures with *Staph. albus* is a very common occurrence, the data recorded here suggest that these same organisms may at times invade the blood stream of certain newborn infants. Contamination from the skin would seem to be an inadequate explanation of the high incidence of positive cultures taken for cause, the regularity with which repeat positive cultures were obtained, the apparent disparity in positive cultures for the various age periods, and the response to therapy.

In suggesting pathogenic and invasive properties to *Staph. albus* we are not unmindful of the fact that this concept is not supported by prevailing opinion. When one considers the scarcity and inconclusive nature of the data pertaining to bacteremia of the newborn infant, prevailing opinion would not appear to be too well supported by fact. The ubiquitous nature of white staphylococci may well account for the unusual frequency with which these organisms are recovered in blood cultures during the neonatal period. The informative study of Torrey and Reese[2] concerning the aerobic flora present in the upper respiratory passages of newborn infants suggests a possible point of entrance. These investigators found that nonhemolytic *Staph. albus* are generally the first organisms to appear in the throat and nasopharynx of newborn infants. In this area they multiply and grow in abundance. It is not unreasonable to hypothecate that when organisms of low pathogenicity are present in abundance they may well overcome the inadequate defenses available to newborn infants and invade the

blood stream in sufficient numbers to result in the syndrome described in this report. The data recorded here would seem to give support to this conception.

The frequent presence of staphylococci in blood samples of healthy infants seems ample proof of the low pathogenicity of the organisms regularly recovered in blood cultures. It is our present practice to test all staphylococci recovered in blood cultures for their ability to produce coagulase. To date all recovered organisms have failed to produce coagulase with one exception. In this instance the organism was identified as hemolytic *Staph. aureus*.

Regardless of what may be a proper interpretation of the significance of the positive cultures described in this study, response to therapy has been too regular to be considered as apparent rather than real. The administration of penicillin and sulfadiazine in the clinical syndrome described has regularly been followed by clinical improvement. In our nurseries the necessity for infusions and blood transfusions has been greatly curtailed.

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SOCIO-EMOTIONAL FACTORS ACCOUNTING FOR GROWTH FAILURE IN CHILDREN LIVING IN AN INSTITUTION

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SOME twenty-five years ago, Holt and Fales,[1] in a classical paper, remarked "that strikingly good health and excellent nutrition can be maintained" in children obliged to live in an institution. These authors were originally stimulated to study the question because of an impression, then prevalent, that "children living in institutions decline in general health and vitality, and that their growth and physical development are inhibited." Holt and Fales, however, then showed that "this is not a necessary result, and that the contrary may be true."

The factors which those authors stressed as contributing to their good results were: (1) regularity in habits of eating, sleep, rest, and exercise; (2) a simple but liberal diet, and (3) freedom from contact infections. The only reference to possible socio-emotional effects is contained in the statement that the children "were happy and gay, not suffering in the least from institutional repression, although they were living under strict regulations."

Such observations have often been confirmed during ensuing years, for it is generally acknowledged that good health and excellent nutrition can be achieved wherever sound institutional management is exercised.

Important as the elements of physical hygiene, medical supervision, and general management obviously are, they are not of themselves sufficient to assure that children in an institution, or for that matter, anywhere, will grow and develop satisfactorily. In fact, in our experience, a crucial role is played by what may be called, for want of a better term "social and emotional adjustment."

SOCIO-EMOTIONAL CONNECTIONS WITH GROWTH AND GROWTH FAILURE: RECIPROCAL RELATIONS

That good socio-emotional adjustment is a necessary condition for good health and good growth now appears to us as undeniable. This conclusion, of course, is not new, but in this paper we shall demonstrate a means of quickly visualizing this interrelationship.

Though professional and administrative officers of institutions have long been familiar with so-called behavior problems, and even though it is routine practice today to be alerted, by way of admission histories, to such possible problems, the connections between physical growth and mental or emotional adjustment are very widely ignored.

To anticipate somewhat the results that are described in the accompanying case histories, it may be said that close, systematic check on physical growth has proved itself to be very helpful in evaluating over-all progress, in indicating

procedure or treatment, and in supplementing clinical impressions of the physician or observations and conclusions by the psychiatrist, case worker, cottage parent, or supervisor. We have learned that evidence of physical growth failure as determined by the Wetzel Grid[2] is an indication of the need for further inquiry concerning emotional disturbances, whereas knowledge of emotional or social tensions as revealed by case records or other sources often leads to further investigation of physical progress and development.

Continued growth failure intensifies the search for physical as well as for psychological causes, and, ultimately, for remedial measures that may even call for temporary change of environment, as described in Cases 3 and 4. On the other hand, reports of improved behavior are checked by observations to determine whether improvement in physical growth has likewise taken place, and if not, to ascertain how that, too, may be accomplished.

In general, attention is paid to physical growth and to socio-emotional behavior for the reciprocal benefit that is to be derived from such coordinated observations. As a result, decisions on program can be formulated with much more than usual confidence. If, for instance, emotional unrest is suspected, a monthly check of the child's Grid record is practically certain to disclose whether the suspected condition is sufficient to affect the child's growth. We are quite confident that a serious emotional disturbance in any child would be manifest on the Grid record of growth when pains are taken to keep that record up-to-date by means of quarterly measurements of weight and height. More attention can therefore be concentrated on those children who fail to maintain the Grid standards of acceptable growth (that is, on those who deviate from an established channel by more than one-half channel for each ten levels of forward advance, and/or who fail to progress at the rate of one level line per month).

A given developmental and/or behavior problem is certain to be more distinctly understood and comprehended by all concerned when that problem situation is judged in terms of the concrete effects which a child's Grid displays concerning his physical growth. This is a result that has been noted not merely by the professional staff, physicians, nurses, psychologists, or psychiatrists and social workers, but also by administrative, supervisory, and other staff members.

In brief, to attempt to deal with a socio-emotional problem in this institution, without benefit of Grid control, is to be working too much in the dark. Similarly, those of the staff primarily concerned with physical growth and with the requirements imposed by growth failure are spared the ignoble error of concluding that, "More calories, more vitamins, etc., might be needed," because they are kept informed of what is going on in the socio-emotional realm of such a child.

It is interesting to note that socio-emotional disturbance can at times exert a sufficiently powerful brake on the natural processes of growth and development to offset every other favorable influence that would normally act to promote and to achieve good growth.*[3] That is a result which becomes especially plain under the conditions of institutional child care, because it is precisely

*The use of the Wetzel Grid in pointing out the connection between social and emotional disturbances and growth failure has been discussed in *Health*, Canada's national health magazine of March, 1948, in an article by Dr. Griffith Binning, entitled, "Peace Be On Thy House."

under those conditions that one has a direct, if not an unique, opportunity to witness good growth existing side-by-side with growth failure, some of which may be unbelievably obstinate. What such experience teaches, above all, is that physical growth progress simply cannot be taken for granted in any child; it must be individually checked upon and controlled, no matter how well a given child may ostensibly appear to be or how perfectly living conditions meet every reasonable standard of shelter, comfort, hygiene, food supply, and other needs of child welfare.

Our studies have been made at Bellefaire, The Jewish Children's Home of Cleveland, Ohio, which is an institution for dependent and neglected children, built on a cottage plan, on a 32-acre parcel in the outskirts of the city. The children come from twenty-seven states, and are in need of group living and psychiatric and case-work treatment. Usually they stay for a period not longer than two years. Many of the children have been placed because of divorce, parental rejection, broken homes, and emotional upheavals in their own homes that created disturbances in their personality. Psychiatric service, case work services, recreational facilities, and living in small cottage groups are geared to provide a therapeutic environment.

An attending psychiatrist, pediatrician, dentist, six case workers, eight cottage parent couples, group workers, psychologist, librarian, and about twelve part-time recreational workers, together with an office and maintenance staff, carry out the work of the institution. The professional program is under the supervision of the head resident.* The agency is merged with the Jewish Children's Bureau of Cleveland, a foster home agency, and the executive director of the Jewish Children's Bureau is also the executive director of Bellefaire.

All children come through social agencies who have made a thorough investigation as to whether the child needs this type of care or other social services.

GENERAL RESULTS

Types of Growth Failure.—Ever since the introduction of the Grid into Bellefaire as a "control chart" on growth some six to seven years ago, and more especially during the past three to four years during which the staff has learned to become more "Grid-conscious" we have had the opportunity of observing practically every type and subtype of growth failure which Wetzel has described in earlier publications. For practical purposes, however, the two most commonly observed types are those associated with (A) simple malnutrition, and (B) obesity. Non-nutritional problems arising from infectious disease, endocrine disturbances, allergy, and as a result of hereditary influences, are occasionally encountered.

As regards origin and treatment, it is a mistake to consider any form of growth failure as due solely to physical causes. This warning we have been abundantly able to confirm. In fact, in dealing with the particular population that resides at Bellefaire, one that has suffered known emotional stress, impact, or strain, we find almost no example without some trace of socio-emotional disturbance, even if it is temporary. Consequently, when growth failure

*Dr. Ralph Fried is the attending pediatrician, and Morris F. Mayer the Head Resident of Bellefaire.

of any kind becomes manifest in a child's Grid, we assume, on the basis of experience, that emotional effects exist, and that these among other things must forthwith be completely investigated and treated.

Obviously, in some instances, the socio-emotional element, though existing, might be of minor importance. In others it may prove to be a formidable barrier to physical recovery which will not be completely achieved until satisfactory emotional balance has been established. In a few instances we have found it impossible to effect recovery from physical growth failure, but it is also in those instances that we have not been able to overcome emotional upset. (Cases 2 and 3).

Incidence.—Physical growth varies with population origin, condition on admission, and adjustment to living at the institution. There have been times when, through adverse coincidence of unfavorable circumstances, demonstrable failure has been identified in 70 per cent of the resident population. As a rule, the fraction of children showing significant Grid deviations that are classified as failure of types A and B is about 40 per cent, that is, just slightly more than the one in three that is known to occur among the general population. This is accounted for by the following facts: (1) lag of even two levels behind expected Grid position is counted; that is, the most rigorous Grid standards are used in order that control may thereby be maximized; (2) failure is deliberately looked for and checked upon by quarterly or even by more frequent re-examination, measurement, and Grid plottings; (3) all children are included, that is, recent as well as longer term residents.

For reasons already explained, 75 to 90 per cent of the children when newly admitted show measurable growth failure, usually of type *A*. Among those who have had six months or more in residence, some evidence of growth failure will be seen in about 15 to 22 per cent. At the present time more than one-half of the total incidence is thus attributable to recent admission. This, however, has not always been the case, because in earlier years, before the advantages of systematic follow-up by the Grid technique had been learned and applied, and during the era in which the tendency to "let nature take her course" held sway, growth failure was about twice to three times as prevalent as now. While it is true that war conditions, notably, constraints imposed by rationing, family separation, casualties, etc., could easily explain 50 per cent or higher incidence, it should be pointed out that "taking growth for granted" was by far the deciding element; for reduction in growth failure to about 22 to 27 per cent of all but recent admissions was accomplished during wartime as soon as Grid control was made to function properly.

In this connection, an incidence of about 50 per cent growth failure has been observed in various private schools. As in our own experience, improvement could likewise be obtained when suitable measures were taken to control a situation that had gotten too far out of hand through the simple assumption that all is well.

In a population of children who have been referred because they are dependent or have been neglected, reduction of the incidence of growth failure

below 20 to 25 per cent will require still more perfect and vigorous control of the chief factors which ultimately lead to such failure in the first place. The incidence of unacceptable growth in an institution of our kind could probably be brought down as low as 7 to 10 per cent, if social and emotional disturbance could be more effectively dealt with than the present state of psychotherapeutic development permits.

Responses and Initial Adjustment.—At least two-thirds of all our children show a flourishing "recovery effect" at the second examination three to six months following admission. This is explained, of course, by the fact that living conditions are much more favorable than those under which these children have previously been obliged to reside.

About one-sixth show normally expected progress and the remaining one-sixth a definite decline in the form of physique loss and level lag. In its severer forms this may amount to as much as two and one-half to three channels and the accompanying level lag may increase to fifteen or even twenty levels. Usually however, a deviation of only one to one and one-half channels is found in the first three months together with lag of about four to eight levels.

Subsequent Course.—Not all of those who respond well to their new environment will continue to develop normally at expected rates. About 10 per cent of the children who make rapid adjustment will later develop growth failure in mild form at the time when the first effects of physical rehabilitation have begun to wear off. These episodes, on the whole, are susceptible to almost immediate control when all concerned have had their attention called to the problem. A few children may be a little more difficult to deal with, and will require somewhat longer to regain their established channels and schedules of development. The remainder, about 2 to 5 per cent of the entire population, or about 20 per cent of any given original incoming group, become the chronic problems upon whom the greatest attention must be centered, but for whom, in the long run, practically the least benefit is to be expected or obtained. We have observed that this group of "physical incorrigibles" consists largely of those children who were too disturbed to benefit from treatment. Some of them had to be transferred to state hospitals or special institutions for unusual disturbances.

From a practical standpoint, our general results may therefore be summed up as follows:

1. Initially or during later residence there is, in most of our children with growth failure, a very striking and close parallelism between this physical affliction and socio-emotional adjustment. Onset and recovery in the one is accompanied quite simultaneously by corresponding progress in the other. The great majority of children who show either, show both, and the disturbances are roughly equal, that is, milder and severer forms of physical growth failure are associated with corresponding degrees of emotional trouble.

2. Dissociated failure, in which anomalous social behavior may either precede or follow evidence of physical lag or channel loss, though less frequent than the foregoing, is probably on the whole more demanding and more difficult to deal with.

The two varieties may be explicitly sketched out: e.g., in the one, physical growth failure will only at some later time be found to be caused by previously unobserved socio-emotional handicaps; contrariwise, in the other, known behavior difficulty will be such as to lead, after an interval, to physical growth slowdown. Similar dissociation is observed during the recovery phases; the psychologists, psychiatrists, case workers, and others will, in one instance, report unmistakable improvement in behavior before a corresponding physical change can be confirmed, or finally, the physician may find, in another child, little or nothing to be desired beyond what its growth and development already show, even though that child's social behavior is still far from acceptable as regards his own or his group living.

3. As for prognosis and treatment, we have learned that in this institution for dependent and neglected children physical growth failure could not be corrected by relying on physical means alone. Had that been possible, growth failure should not have appeared at all in an environment where efforts to provide shelter, food, and living enabled a good majority of youngsters, similarly experienced, to grow and develop satisfactorily. Additional calories and vitamins with which to pay off "fuel debts" were never of themselves sufficient to induce and to effect recovery until a feeling of security, and simultaneously with that, emotional tranquility, could also be firmly established.

CASE HISTORIES

To provide concrete illustrations of our main findings, four case histories are reviewed briefly. All show the simple nutritional type of growth failure (*A*) since this, in our experience is much more troublesome to deal with in emotionally disturbed dependent children than the obese form *B*. Even as few as four such examples are sufficient to demonstrate (a) that emotional adjustment and physical growth are inseparably related; and (b) that Grid control is a simple and remarkably exact means of helping to check on progress and on results.

These examples taken in order show: (1) prolonged initial adjustment; (2) delayed, intractable, and progressively more serious maladjustment; (3) recurrent failure; and (4) interrupted care, with full recovery on a second admission.

CASE 1.—Paula was 8 years, one month old when she entered Bellefaire shortly after she had been deserted by her mother, who had suffered a psychotic breakdown subsequent to the birth of a deformed child. Up until then, Paula had lived in a fairly well-established family for which the father had shown great interest, and among whom only minor friction took place. Though the mother was emotionally unstable, she had taken good care of the girl. The mother's breakdown had been sudden, the family separation equally so, with the result that it took the child almost two years to become oriented and adjusted to realities.

During the three months following admission Paula was in a daze. Coincidentally she dropped from level 77 to level 69, though failure to eat was not responsible. This loss of eight levels of development actually put her eleven to twelve levels in arrears at the end of that period, because she should have reached level 79 or 80 according to normal expectancy.

She gradually made friends, and was gradually accepted among the children. When

her infant brother was placed in the nursery cottage, she took an interest in him and learned to love him in spite of his deformity. Intensive case work was given during that whole period.

During the mother's convalescence, which took about a year, the father maintained a close and uninterrupted interest in the girl. When the mother returned, recovered from her psychotic episode, she accepted her daughter as she had always done, and was helped to take an interest in the baby. This led to a reunion between father and mother, and thereupon to an awareness on the child's part, that she could soon return to her home. The over-all trends in the Grid record (Fig. 1) closely parallel Paula's progressive adjustment to institutional life, which required a year and one-half to become satisfactorily established.

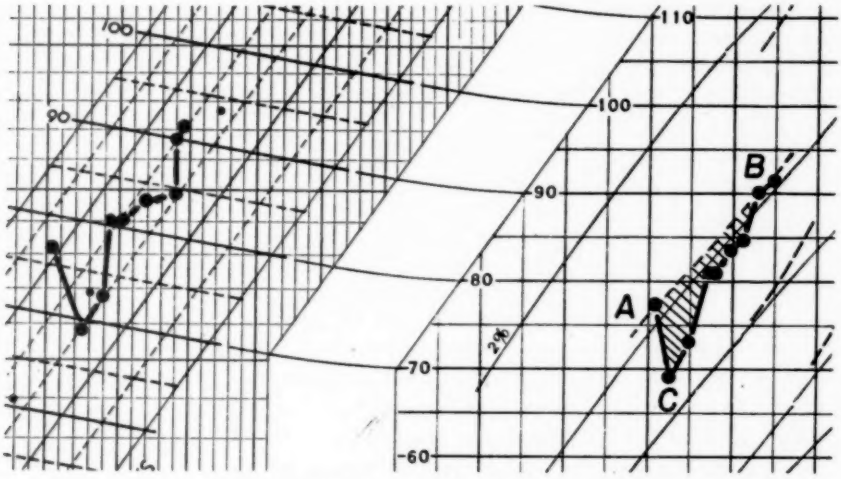

Fig. 1.—Paula. *A-C* represents the initial growth failure on admission to Bellefaire. At *A* Paula was 8 years one month old. At *C* she was 8 years, 4 months old. *C-B* represents the recovery period as the child adjusted to Bellefaire.

It is particularly important to emphasize that the *amount* and *kind* of growth failure which her Grid shows *could not* (and ordinarily would not) be recognized by clinical examination, because she never slipped below channel *M*. Her bodily contours were still such as to inspire the impression of "good nutrition," "good physical condition," etc. In situations such as hers, that conclusion would be erroneous; and it would be so because the comparatively good appearance of children in *M* tends to mask any accompanying failure even when that is as great as Paula's was, and as plainly manifest as it is in her Grid record.

CASE 2.—Sol entered Bellefaire three days after his seventh birthday, along with his brother who was 11 years old. Both were very bright children; each had an I.Q. of about 140. Their parents had been divorced, an act that confused and disturbed both boys, who were deeply loyal to their father. For the latter reason, the referring agency had recommended institutional rather than foster home placement, but the agency also recommended that institutionalization should be no longer than one and one-half to two years, since it sensed that the boys should not be deprived of the benefit of a private home, this being especially true of the younger.

Sol made a good adjustment during the first year and one-half. Then he had progressively more serious difficulties at Bellefaire. He started out as, and has continued to be, a leader in his group, whose respect he commanded even though he was one of the smallest boys of the group.

The plan to place him in a foster home after a year and one-half was thwarted by two circumstances: no suitable foster home was then available, and both parents strongly resisted that suggestion. As a result Sol was obliged to remain under institutional care. He showed some behavior disturbances and gradually became involved in various difficulties. He developed a definite negativistic attitude, and for the past two and one-half years has merely been "marking time," in spite of an outward appearance of making a good adjustment to institutional life. All attempts of the social workers and psychiatrists to get close to him, his brother, and his parents, and to arrange foster home placement have thus far been unsuccessful.

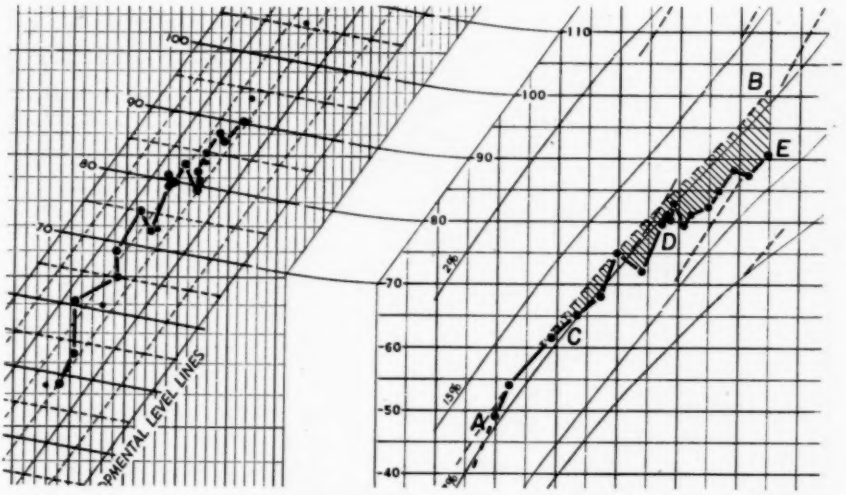

Fig. 2.—Sol. Initial adjustment during the eighteen-month period, *AC*, was good. Minor difficulties at *C* only partially controlled up to *D* when he should definitely have left the institution. *D-E* represents continued deterioration. *AB* is the course he should have followed.

Sol's Grid record (Fig. 2) clearly reflects the result of all of the foregoing. From this record it is evident that he should have left the institution at about the age of 9 years, for it is plain that institutional living has not been able to prevent or to overcome what has developed, under the circumstances, into moderate and even moderately severe growth failure. From a practical standpoint, still further trouble is all that can justifiably be expected by continued residence here.

It should be noted that Sol was a boy who progressed along the central *M* channel and that he, accordingly, always gave the impression of being quite sturdy and well built. In fact, when he was examined objectively by several physicians, none suspected that he was actually under par or in a state of growth failure that amounted to six to twelve levels of development.

CASE 3.—Alvin entered Bellefaire when he was 9 years, 11 months old, and shortly after the separation of his parents. The father had been periodically addicted to drink, was a poor provider, and finally deserted the home. The mother was employed in a defense factory, and an older brother was in the service.

During his first six months Alvin seemed to make a good socio-emotional adjustment, and on the physical side, gained thirteen levels in a recovery response that carried him from levels 97 to 110. This clear-cut improvement was apparently due to relief from domination by a particularly strong-willed mother who had "always tried to run his life."

Indeed, his early behavior was characterized by an overly submissive compliance to ordinary rules and regulations. Yet the staff soon suspected that he would prove to be a severe problem because his mother made deliberate efforts to interfere with his institutional adjustment. He became involved in numerous delinquencies and showed no guilt feelings. At the age of 12 years and 3 months he had fallen at least twelve levels (or about a year) behind his own schedule of development. In order to treat this moderate growth failure, which seemed destined to get worse unless things changed radically, he was referred to the Children's Fresh Air Camp of Cleveland, a special institution for children with growth deficiencies.

In spite of only a brief stay there, which had to be terminated in two months because of troublesome behavior, he improved promptly on the physical side, with a gain from level 116 to level 126. (Fig. 3, *C-D.*)

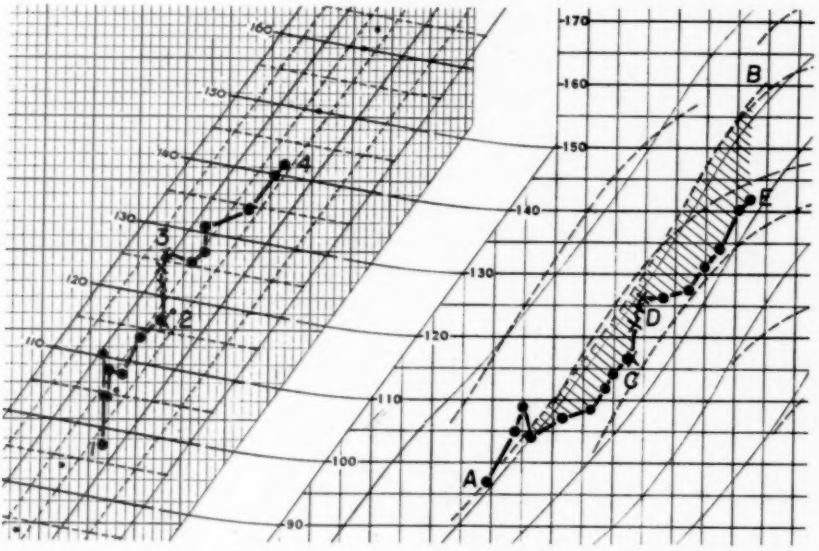

Fig. 3.—Alvin. As noted on the chart, the boy's initial response was good. Growth failure starts and continues to point *C* at which time he was placed on a special health regime in another institution. *C-D* represents recovery at F.A.C. On return to Bellefaire he continued to fail to point *E* instead of reaching expected point *B*.

As definite and as obvious as this response was, it fell about 4 to 6 levels short of complete recovery. His emotional reactions, however, showed no corresponding improvement, with the result that a permanent improvement on the physical side did not occur.

His physical progress halted as promptly as it had previously begun; in the eleven months following readmission he made the "isodevelopmental shift" along levels 126 to 127, gaining, at the most, only one and one-half levels in about a year! He became practically inaccessible to any approach for psychotherapeutics. In this regard, it is noteworthy that he had never been able to form any attachment to an adult during his entire five-year residency here. Lacking such an attachment, he made little more than superficial attempts to improve, and these were, again, overly submissive. Invariably, he fell back into delinquencies and regressive behavior patterns.

In Alvin's case, emotional disturbance and physical growth failure are certainly related as direct cause and effect. It is evident to us that physical means alone cannot succeed in overcoming his growth failure, which becomes ever more serious as he approaches the time of epiphyseal union. In view of the partial recovery he was once enabled to make,

the outlook for full recovery would by no means be unfavorable, but the outcome itself will depend, as much as ever, upon his adjustment in some favorable socio-emotional environment.

Alvin's physical appearance in the examining room belied his true status and progress. He never gave the impression of being actually "under par" though he did look better after his partial recovery to A_1-126. Without the Grid record he would have been passed repeatedly with negative findings.

CASE 4.—Joseph has been in the institution on two occasions separated by a one and one-half year interval spent in foster homes. His first entry to Bellefaire began when he was 6 years, one month old, and lasted for three years. It was unsuccessful in practically every respect; his second entry, at the age of 10½ years, has now lasted almost two years and it has provided a complete recovery from serious growth failure, as well as an all but complete socio-emotional adjustment to this same environment.

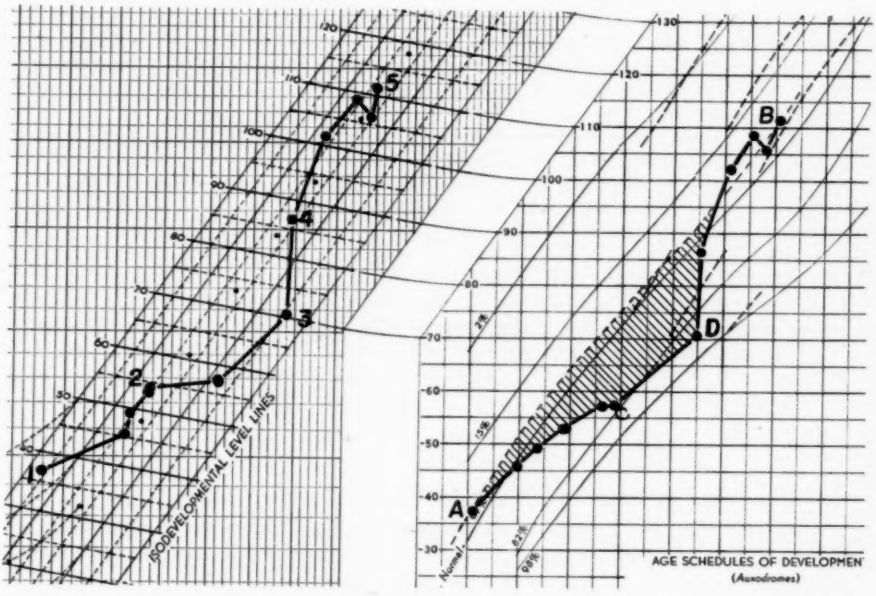

Fig. 4.—Joseph. At *A* he was 6 years old and his unsuccessful adjustment is shown by growth failure which continued until discharge at *C*. It continued in his own home and foster homes until *D*, when he was readmitted to Bellefaire. This time he made a successful adjustment and reached his expected level at *B*.

Joe, whose father had died when the boy was still an infant, originally entered Bellefaire following a series of failures in foster homes. These were caused primarily by interference of his mother, although she herself had no competence as a homemaker.

Joe was a greatly disturbed and confused boy who could make no really satisfactory adjustment at any time during his first three-year stay. His behavior fluctuated between the extremes of withdrawal on the one hand to hyperactivity and aggression on the other. His life at the institution was repeatedly upset by his mother's interference, which led to many unpleasant experiences. Unhappily, the boy was torn between loyalty to his own and to his cottage mother. The former finally insisted that Joseph and his sister return home, something both children desired to do.

During his first three years at Bellefaire, Joe had progressed from level 36 to 57, that is, only twenty-one levels in thirty-six months, and much farther to the slender side of the

channel system than his earlier course would normally have suggested. He had actually fallen at least twenty levels behind his scheduled development since he should have reached level 77 along his expected auxodrome.

His mother's efforts to support and maintain a home for the children lasted only about a year. Joe and his sister were again placed in foster homes, but again without success. Thus, after one and one-half years' absence, both returned to Bellefaire. Joe was given intensive psychiatric treatment for his known negativism; the case worker took immediate and thorough charge of his social wants, and Joe himself developed a remarkably close attachment to his cottage father. He remained aloof from most people, however, for a long time, but gradually developed a much more acceptable and positive attitude toward others. His delinquencies decreased, his school marks improved, and he obviously became a happier boy. He has actually emerged as one of the leaders of his group, although his adjustment is not yet sufficiently stable to permit him to be a consistent or an always constructive influence among them.

Joseph's physical improvement was even more pronounced than that which he showed on the emotional side. As his Grid shows, his recovery from physical growth failure became complete within eight months of his second admission. It was complete in the sense that he had, even then, returned to par by advancing thirty-one levels from 71 to his own channel at level 102.

While psychological and physical changes did take place coincidentally, the former were, on the whole, the more rapid and the more immediately tangible. Once physical repair had set in, moreover, there was every reason to expect all of the psychological improvement he has ultimately shown. Both effects in this instance are, in a sense, the result of a kind of favorable "shakedown" which took place during his temporary absence between admissions. Otherwise, his second entry would more likely have resulted, through memory association, in repetition and furtherance of his original failure. The first admission had not proceeded satisfactorily and Joseph's power to react to efforts that were made to help him had apparently waned; his outside experience with his mother's unsuccessful efforts and with those at foster homes might easily be interpreted as having cleared the air in preparation for renewed life among the institutional group with whom he had been familiar. In any case, socio-emotional adjustment, however achieved, was a necessary condition to his recovery from physical growth failure.

DISCUSSION

The foregoing case histories, taken in conjunction with the records of growth progress as revealed by the accompanying Grids, clearly demonstrate the practical value of such direct and objective follow-up. In each example the Grid trends are definite despite the minor fluctuations they contain. There is, accordingly, no difficulty in deciding which deviations are actually significant or which should be considered as accidental.

A single glance, at the time of each successive checkup, reveals the *kind* and the *amount* of progress that has been made, not in the quite meaningless terms of height or weight changes, but rather in concrete effects such as change in physique, level gain, remaining lag, and calorie deficits. The first two of these can be checked by direct examination and inspection of the child, and when so employed, they can help to substantiate clinical impressions. The latter two findings serve as a basis for prognosis and for therapeutic plans. Thus, whether the child's Grid be viewed as a whole, or for separate detail, it registers the net effect not merely of what has been going on or of what has been accomplished, but it indicates to physician, nurse, case worker, and cottage parents alike what still remains to be achieved. Expressed as it is, in

terms of physique and size, direction, and speed of growth, it actually penetrates the external camouflage that is put on by many children at the time of their checkups.

From even the four examples we have described, it is evident that socio-emotional impacts which disturb growth at all are more than ordinarily serious. In the first place, the appearance of growth failure actually demands the solution of two, not simply of one, clinical problem. Second, growth failure, once initiated, always tends to become worse, regardless of cause. From an institutional standpoint, both of these effects imply added responsibility and care, just as they do under normal family circumstances. When, in an institution, some 20 to 30 per cent of the residents are bound to be affected, and it seems unwise to reckon on less than this in a group of dependent children, difficulties of management and control are certain to mount very rapidly, not to mention the extra load imposed on staff time and effort or the inevitable increase in per capita costs.

For these reasons the benefits of early recognition of failure and of continuing evidence on what degree of control is being achieved hardly require further emphasis or explanation. In any case, socio-emotional disturbances are matters of very real concern and they are, for the most part, none too easily dealt with even when they occur or appear to occur alone. When they persist and incite physical growth failure, as they often do, they become matters for still greater concern. In this situation, we have found it advantageous to make use of the reciprocal actions between emotional upset and growth failure for the purposes of achieving what the institution itself had been established to provide. To this end, individual control on growth as exercised through quarterly, or, when necessary, by more frequent Grid follow-up, has been made an essential part of each child's management, supervision, and care.

SUMMARY AND CONCLUSIONS

1. From observations made in an institution that cares for dependent and neglected children, we have been able to demonstrate that socio-emotional adjustment plays not merely an important but actually a crucial role among all the factors that determine individual health and physical well-being.

In the present study (a) anecdotal matter on behavior is supplemented by, and correlated with, (b) medical findings on health, (c) psychiatric evidence, and with (d) quarterly evaluations of physical growth and development, the latter with the aid of the Grid technique described by Wetzel.

2. From combined evidence of this kind, it has become clear that socio-emotional disturbance tends to affect physical growth adversely, and that growth failure so caused is much more frequent and more extensive than is generally recognized.

3. The most favorable conditions of shelter, spacious grounds, food supply, schooling, medical protection, and supervised social life in such an institution are themselves not sufficient to assure good physical growth and development of its children. All these things are as nothing until equable social adjustment

can be established. When, however, that is accomplished, growth and development among institutionalized children proceeds just as satisfactorily as it ever does, and according to the standards of direction and speed indicated by the Grid technique.

4. For obvious reasons, the incidence of simple growth failure is comparatively high among children who are institutionalized owing to dependency or neglect. Among new admissions, it is practically 100 per cent; thereafter, incidence depends (1) on vigilance and proper action, and (2) on the degree to which disturbance can be controlled.

5. Features of initial and delayed adjustments, recurrent failure, and the occasional advantage of change in environment are described in four case histories illustrated with their respective Grid records. The most general result these examples demonstrate is the cause-and-effect reciprocal relation between socio-emotional disturbance and physical growth failure.

6. Regarding the Grid technique itself, certain specific advantages have become apparent. Besides serving its original purpose as a "control chart on physical growth" and thereby supplementing clinical estimates of physical condition and progress, the Grid has proved itself valuable as one guide to coordinating the work of the whole institution to the end that the individual's needs may be most effectively met. This means that the Grid helps to confirm the specialized impressions gained by social workers, psychiatrist, pediatrician, nurse, and supervisors, and that it provides these different staff members with a common basis for understanding their common problems. To all of these it has become the simplest and most accurate method of conveying and of making plain what the current end result on growth in any given child should signify. This advantage helps to secure a more intelligent balance between individual and group needs, on the one hand, and institutional program and facilities on the other.

7. Apart from individual consequences, growth failure adds to the burden as well as to the cost of institutional care, and it subtracts from the results which such an institution is intended to achieve. Faced as it is with the difficulties that emotional upsets themselves impose and with the fact that emotional adjustment and physical growth are profoundly related, the need for early recognition of trouble, prompt action, and periodic appraisal is beyond debate. To this end, individual control on growth as exercised through quarterly, or, when necessary, by more frequent Grid follow-up, has been made an essential part of each child's management, supervision, and care.

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FOOD ALLERGY

Death in a Six-Day-Old Infant

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THE case to be presented in this paper is unique for the following reasons: (1) The child was one of the youngest to die because of food allergy who has ever been reported in the literature. (2) Death was precipitated by allergic shock following the introduction of an amino acid food. (3) Although, since birth the infant had purposely been given such foods as soybean milk and goat's milk (nonallergenic usually), nevertheless he reacted promptly and severely to them. (4) Finally, because of the sibling history, catastrophe was anticipated and, despite forewarning, was apparently unavoidable.

CASE REPORT

J. T., a white male infant, was admitted to the Jewish Hospital on the service of one of us (R. A. S.) Nov. 4, 1946 at 8:30 P.M. The baby was 6 days old and was born at full term. The mother's pregnancy had been uneventful. Delivery was normal. The birth weight was 7 pounds and 2 ounces. The mother had given birth to a baby several years previously—her first—who died twelve days following birth as the result of severe food allergy, manifested by eczema and diarrhea. This first baby had nursed and also had taken evaporated (cow's) milk as complementary feeding. Because of the sibling history, special attention was paid to the management of this newborn baby in an effort to avoid another catastrophe. It was decided to avoid breast and cow's milk feedings altogether, and consequently nonallergenic milk in the form of Mull-Soy (soybean milk) was used. The baby was taken home on the day of birth and placed under the care of a special nurse with the type of milk mentioned. In spite of this planned program, the child immediately began to develop a facial eczema, which became progressively worse. The infant also regurgitated several feedings a day and vomited large quantities of mucus. He started to show some weight loss. Two days later he developed frequent bowel movements, having seven to nine well-formed stools in twenty-four hours. The next day the baby began to pass a great deal of mucus by bowel. Weight loss was progressive. The picture looked just as it had with the first baby, in spite of the forewarning. Then goat's milk feedings were tried, but with no improvement. Hospitalization was decided on for the purpose of parenteral feedings.

In the family history, in addition to the death of the sibling, it was significant that the father suffered from asthma and the mother from eczema and neurodermatitis—a strong allergic background from both parents.

Physical examination revealed a very thin, malnourished, white male infant weighing 6 pounds and 8 ounces (loss of 10 ounces in the six days following birth). The rectal temperature was 99° F. The baby was lying rather quietly and in no acute distress. The face, scalp, forehead, and groin were covered with scaly, eczematous patches. A purulent exudate was present in both eyes. The pupils were normal. The auditory canals were filled with scales on the walls and external openings. The posterior wall of the oropharynx was moderately erythematous and showed a purulent exudate. The chest revealed some coarse râles throughout the lung fields. The heart was normal. The abdomen revealed no tenderness. Peristalsis was normal. The liver, spleen, and kidneys were not palpable. The extremities were normal and showed no pathologic reflexes.

From the Department of Pediatrics, Jewish Hospital.

The urine was yellow and cloudy with a pH of 7.0 It contained plus two albumin, a faint trace of sugar, and an occasional white blood cell per high power field. The blood contained 18 Gm. of hemoglobin, 5.44 million red blood cells, and 31,200 white blood cells with 68 per cent polymorphonuclear cells and 32 per cent lymphocytes. Of the white cells, 41 per cent were filamentous neutrophiles and 59 per cent nonfilamentous.

The baby was immediately given a continuous intramedullary infusion (tibia) of 5 per cent amino acids with 5 per cent dextrose (Amigen)—a total of 500 c.c. slowly at the rate of 10 drops a minute to avoid speed shock. In addition, 2 ounces of 5 per cent glucose in half-strength normal saline were given orally. Oxygen was administered, and ascorbic acid, 25 mg., was given twice daily.

The baby received all the Amigen and two hours later was being prepared for a transfusion, when at 2:15 P.M. (the day following admission) he suddenly expelled frothy, yellowish mucus from the nose and throat. He appeared cyanotic, became stuporous, dyspneic, and in extremis. Aspiration was immediately performed, oxygen was given by mask, and 3 minims of epinephrine (1:1,000) and 2 gr. of caffeine sodium benzoate were injected subcutaneously. There were many bubbling râles audible throughout the chest, and the heart sounds were not audible at this time. After receiving the epinephrine the respirations became deeper, the cyanosis diminished, and fifteen minutes later, when the chest was again examined, the respiratory sounds were quite clear. The heart rate was 66 per minute and the respirations 40 per minute.

At 4:30 P.M., the infant was deeply stuporous and slate-gray in appearance. The eye movements were jerky with several myoclonic contractions of both upper extremities. The respirations were again moist. The heart rate was irregular and 112 per minute. The epinephrine was repeated and heat applied to the extremities. The transfusion of blood had been canceled meanwhile, the baby not having received any at all.

At 5:15 P.M.—less than twenty-four hours after admission—the baby expired.

The clinical impression obtained was that the baby had died from anaphylactic shock precipitated by the Amigen. This was based on the history of the strong allergic background of the parents, plus the sibling death, plus the eczema and diarrhea (allergic reactions to the usually nonallergenic milks), plus the exciting factor (Amigen) which undoubtedly caused the secretion of mucus from the nose, throat, and bowel, and the edema of the lungs, plus the favorable response to the epinephrine, which unfortunately was only temporary and insufficient to avert death.

Autopsy Findings.—At necropsy, a moderately emaciated infant, weighing 2,700 Gm. and 18¾ inches long, showed erythematous, eczematoid, crusted lesions on the face and forehead down to the neck. The nail beds showed marked cyanosis. The lungs revealed emphysematous areas and purplish mottling. On section, there was evidence of much congestion and edema. The gastrointestinal tract showed submucous hemorrhages in the esophagus and congestion of the entire mucosa of the stomach and small and large intestines. There was a great deal of congestion in the liver, spleen, kidneys, adrenals, pancreas, bone marrow, and brain, visible grossly as well as microscopically.

The cause of death was severe allergy. The shock organs were the skin, gastrointestinal tract, lungs, liver, and brain. The immediate cause of death was pulmonary. The lungs showed hemorrhage and edema due to anaphylactic shock.

DISCUSSION

That allergy is common in the newborn infant is not a new concept. Campbell,[1] in reporting 200 cases of allergic children, revealed that 25 per cent had symptoms during the newborn period. Glaser[2] further noted that the following signs and symptoms were present at birth or shortly afterward in allergic infants: anaphylactic shock from human milk, infantile eczema, cough, colic, vomiting, wheeze, postauricular intertrigo, dry and ichthyotic skin, edema of hands and feet, seborrhea, excessive sneezing, rhinitis, and excessive hunger.

Clein[3] reported that the first allergic symptoms appeared in 39 per cent of 100 allergic children in the first month of life, and in 24 per cent, 13 per cent, and 6 per cent respectively in the following three months. The possibility of anaphylaxis caused by human milk is illustrated by two of his cases:

> "A newborn infant whose older brother had died of anaphylactic shock after his first breast feeding presented similar symptoms when one drop of his mother's milk was placed on his tongue. He was promptly weaned. One month later, he reacted strongly positive to human breast milk.
>
> "Another infant, on being placed to the breast on the second day of life, went into a state of anaphylactic shock so severe that the head nurse baptized him during the episode. He was resuscitated by epinephrine and artificial respiration. The same thing occurred on the following day when he was given one drop of his mother's milk. He was proved allergic to human milk by skin testing."

McLendon and Jaeger[4] listed the symptoms in the syndrome of milk intolerance as follows in the order of frequency with which they occur: constipation, anorexia, abdominal discomfort, pallor, fatigue complex with lassitude, disturbed sleep, recurrent diarrhea, respiratory and urinary disturbances. The characteristic features of the history obtained in these cases are: family history of allergy, excessive milk ingestion during the later months of pregnancy, early ingestion of cow's milk by infant, colic syndrome, and frequent formula changes with only transient relief following such changes.

Most allergists and pediatricians feel as Glaser[5] does, that the best substitute for these allergic infants, whether the offender is human or cow's milk, is soybean milk. He has shown dramatic improvement in his patients where the cow's milk has been eliminated and the substitute given. It did not work in our case, however.

Many investigators in seeking an explanation for sudden death in allergic infants have advanced different concepts. At one time, the cause for sudden, unexplainable death in an infant, whether of an allergic background or not, was attributed to an enlarged thymus. This has of recent years been disproved. Feer[6] described this so-called concept of status thymolymphaticus or suffocation by a suddenly enlarged thymus gland. The English Status Lymphaticus Investigation Committee, after performing autopsies on 600 newborn infants who had died suddenly, questions the existence of a thymic diathesis and considers these deaths the result of anaphylactic shock.

Davies[7] in 1940 reported the fatal outcome in three cases of infantile eczema, the children aged 4, 6, and 8 months, respectively. In his cases the following picture was presented: The first definite change noted was restlessness, then dyspnea, and then in some cases Cheyne-Stokes respirations. Vomiting was frequent and convulsions occurred. The temperature became elevated (103° F. or higher rectally). The infants became unconscious, the lips blue, the skin livid, and the extremities cold—all evidence of shock. He attributed

the deaths in large measure to the psychologic trauma of separating the infants from their mothers.

It is interesting to note that some observers like Epstein[8, 9] believe in the theory of Sulzberger—namely, that where local medication is used extensively for the eczematous lesions, phenol poisoning from coal tar in combination with an interference with cutaneous respiration and the instability of the autonomic nervous system would explain the symptoms as well as the other circumstances of acute death from allergy. (In passing, we wish to state that no tar or any local medicine was used, because we felt that the condition was too widespread and systemic in origin to yield to local therapy.)

Huttinel and Rever[10] compare the clinical picture in fatalities from allergy to the experimental condition in animals and believe that anaphylactic shock would explain the pallor, syncope, dyspnea, and convulsions.

Waldbott[11] also confirms this opinion and points out that in all autopsies on patients who have died from allergy the lungs present, uniformly, congestion, extravasation of blood, and edematous fluid. Death is caused by the edema of the lungs and the ensuing asphyxiation, and it is well known that edema is a definite characteristic of allergy and anaphylaxis.

Leopold,[12] pediatric allergist at our hospital, states that soybean sensitivity, although uncommon, does occur. It may well be that there was some hypersensitivity transmitted to the baby via the placental circulation as the result of the mother's diet during her pregnancy. Soybean is found in many items such as bakery goods (bread, cakes, rolls, and crisp crackers), sauces (Heinz and Lea and Perrin's Worcestershire sauce), salad dressings and mayonnaise, pork sausage and lunch meats, candies, Crisco, Spry, and other shortenings, and oleomargarine and other butter substitutes. In addition, Leopold indicates that Amigen, itself, may be a protein offender. Harris and his associates[13] have reported a case of sensitivity to Amigen (nonfatal) with anaphylactic manifestations in an adult to whom it was given intravenously, following barbiturate poisoning. Leopold points out that Amigen is the product of pancreatic hydrolysis of casein. Although it is theoretically composed of amino acids and polypeptides, only 65 per cent of the nitrogen in Amigen is amino acid nitrogen, the rest being nitrogen of higher amino acid groupings. It is possible that Amigen may contain higher groupings such as proteoses of casein, which may have caused the anaphylaxis in this case. Dr. Robert Cooke, the eminent allergist, has reported allergic reactions to proteoses of milk.

SUMMARY

1. A fatal case of food allergy in an infant 6 days old is presented.

2. Because of the death of a sibling due to similar allergy, trouble was expected. To prevent another death, the infant from the beginning was placed on nonallergenic milk only. In spite of this precaution, he reacted severely.

3. As a last resort, amino acid food was given. This, however, only served to hasten his death by causing further severe protein shock.

CONCLUSION

The most likely inference is that this infant was sensitized to all forms of protein during its fetal life. We took no chances with protein foods which are possible offenders—namely, human and cow's milk—but instead used hypoallergenic milk such as goat's milk and the soya bean variety, assuming that they would be safe. When these failed, simpler proteins such as those found in Amigen were tried, but to no avail. It is axiomatic that protein is essential to life. Since it was impossible to supply it in this case, even in the simplest forms available, without dire results, it is difficult to see what nourishment would have kept alive such an extremely allergic infant.

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ERYTHROCYTE SEDIMENTATION RATE DETERMINATIONS IN POLIOMYELITIS AND OTHER INFECTIONS OF THE CENTRAL NERVOUS SYSTEM AND MENINGES

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INTRODUCTION

THE variability and nonspecificity of the erythrocyte sedimentation rate* are well known.[1, 2] Previous reports[3, 4] have pointed out the variations in the erythrocyte sedimentation rate in acute poliomyelitis but have, at the same time, emphasized the value of this determination as an aid in the diagnosis of the disease. Because of the problems in differential diagnosis which are frequently presented by abnormal findings in the spinal fluid, it was decided to evaluate the sedimentation rate as a diagnostic procedure on all patients who presented clinical evidence of meningeal irritation or who had abnormal spinal fluid findings. The present report is concerned with erythrocyte sedimentation rate determinations on sixty-five poliomyelitis patients during the acute and convalescent phase of their disease and also acute phase sedimentation rate determinations on forty-six patients who had abnormal spinal fluids, some of which presented a problem in diagnosis. Twenty-six patients who had questionable clinical evidence of meningeal irritation or who were thought to have central nervous system disease disproved by lumbar puncture and clinical course were used as controls.

TABLE I. POLIOMYELITIS ERYTHROCYTE SEDIMENTATION RATES*

TYPE POLIOMYELITIS	NO. CASES	ESR ELEVATED ON ADMISSION	ESR ELEVATED 1 WEEK AFTER ADMISSION	ESR ELEVATED 2 WEEKS AFTER ADMISSION	ESR NORMAL ON ADMISSION, THEN ROSE
Bulbar	11	3	5	2	3 of 8
Paralytic	28	17	7	5	0 of 11
Nonparalytic	26	13	3	1	0 of 13
Total	65	33	15	8	3 of 32

*Because practically all the erythrocyte sedimentation rates had returned to normal by the third determination, only three determinations have been listed in this table.

MATERIALS AND METHODS

Erythrocyte sedimentation rates were performed on all individuals found to have abnormal spinal fluid who entered the Haynes Memorial Hospital during the period from July 1, 1947, to April 30, 1948. Of these, sixty-five (twenty-one adults and forty-four children) had conditions diagnosed as poliomyelitis and forty-six (eighteen adults and twenty-eight children) had abnormal spinal fluid findings due to other causes (See Table II).

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*The terms erythrocyte sedimentation rate, ESR, sedimentation rate, and fall in red blood cells are used synonymously in this report.

TABLE II. ERYTHROCYTE SEDIMENTATION RATE DETERMINATIONS IN INFECTIONS OTHER THAN POLIOMYELITIS

GENERAL TYPE	SPECIFIC TYPE	NO. CASES	ADMISSION ESR'S	
			NO. NORMAL	NO. ELEVATED
Suppurative meningitides	Meningococcus	7	0	7
	M. tuberculosis	3	1	2
	Hemophilus influenzae	7	3	4
	Staphylococcus	2	1	1
	Pneumococcus	1	1	0
	Streptococcus viridans	1	0	1
	Torula	1	1	0
Viral and post-infectious encephalitides	Mumps meningocephalitis	11	8	3
	Post-measles encephalomyelitis	6	2	4
	Post-varicella encephalomyelitis	1	0	1
	Post-rabies vaccine encephalomyelitis	1	1	0
Meningitis due to other causes	"Serous meningitis"	2	0	2
	Lead encephalitis	2	2	0
	Cerebellar hemorrhage	1	1	0
Total		46	21	25

Twenty-six patients (seven adults and nineteen children) who were thought to have clinical evidence of meningeal irritation or central nervous system disease but who were found to have normal spinal fluid were used as controls. The final diagnosis and number of normal and abnormal sedimentation rates at the time of admission to the hospital are listed in Table III. Some of these patients may have had abortive poliomyelitis, but this diagnosis could not be established definitely.

TABLE III. UNCONFIRMED CENTRAL NERVOUS SYSTEM DISEASE SUSPECTS WITH MENINGEAL SYMPTOMS

FINAL DIAGNOSIS	NO. PATIENTS	ADMISSION ERYTHROCYTE SEDIMENTATION RATE	
		NO. NORMAL	NO. ELEVATED
Upper respiratory infection	4	3	1
Hysteria	4	4	0
Myalgia	4	2	2
"La grippe" syndrome	4	1	3
Pneumonia	3	0	3
Bacteremia	1	0	1
Trichinosis	1	0	1
Rheumatic fever	2	1	1
No disease	3	3	0
Total	26	14	12

A modification of the original Westergren[5] technique was used for the determination of the erythrocyte sedimentation rate; 3.0 ml. of freshly drawn blood were mixed with 0.75 ml. of 3.8 per cent sodium citrate solution and the mixture drawn up in a Westergren tube to a height of 200 mm. and placed upright in a leveled stand. The fall in red blood cells was measured one hour after the test was set up. The normal range of red blood cell sedimentation with this method is 0 to 15 mm. for male subjects and 0 to 20 mm. for female subjects in one hour.

Weekly erythrocyte sedimentation rates were performed on all patients with poliomyelitis. The determinations on patients with other types of central nervous system infections and on those patients suspected of having neurologic disease were performed usually only on admission since the purpose of the determination was to evaluate its early diagnostic significance.

RESULTS

Of sixty-five patients who had a clinical course and spinal fluid changes consistent with the diagnosis of poliomyelitis, thirty-three had elevated sedimentation rates at the time of admission to the hospital. Of these the elevations in three were accounted for by pregnancy, in one by diabetes and in another by pansinusitis. Although many had only slight elevations in their erythrocyte sedimentation rate (1 to 10 mm. above normal), others showed increases as high as 25, 28, and 55 mm. in uncomplicated cases. At the end of the first or second week most of the sedimentation rates had returned to normal levels (See Table I). There was no correlation between the type of poliomyelitis, severity of the disease, or degree of abnormality of the spinal fluid and the sedimentation rate. Only three patients had an elevated rate following a normal admission rate. These findings are in essential agreement with those previously reported for poliomyelitis,[3] but are not in agreement with the small number of elevated sedimentation rates in the acute phase of poliomyelitis as reported by Fox and Evrard.[4]

Forty-six patients who had abnormalities of the spinal fluid due to diseases other than poliomyelitis are listed in Table II. Of twenty-two who had bacterial infections involving the meninges, the admission sedimentation rate was elevated in fifteen and normal in seven. Eleven of nineteen postinfectious or viral encephalitides had normal rates while eight were elevated on entry to the hospital. Two of five patients with an abnormal number of cells in the cerebrospinal fluid due to miscellaneous causes had elevated sedimentation rates.

In twenty-six patients who were referred to the hospital with equivocal findings of meningeal irritation but who had no laboratory or clinical evidence of disease of the central nervous system, the ESR was normal in fourteen and elevated in twelve.

DISCUSSION

The variations and nonspecificity of the erythrocyte sedimentation rate are well known. Although it is generally accepted that the erythrocyte sedimentation rate may be either elevated or within normal limits in the early stages of many of the infectious diseases, the value of this determination in early poliomyelitis has been stressed.[3, 4] Because of the problems of diagnosis which abnormalities of the cerebrospinal fluid may present and also because of the frequent urgency of making a prompt decision as to whether an instance of neurologic disease is viral or bacterial in origin, an attempt has been made to evaluate the erythrocyte sedimentation rate as a diagnostic aid in making such a differentiation. The results of the present study would seem to indicate that in acute poliomyelitis the erythrocyte sedimentation rate initially may be

elevated, but that in general, the uncomplicated course of the disease is usually marked by a normal rate. This is in general agreement with previous reports.[3, 4] Frequently, however, a case of nonparalytic poliomyelitis with a large number of cells in the spinal fluid early in the disease may raise the possibility of an early bacterial meningitis. It was hoped, early in this study, that the erythrocyte sedimentation rate might help in differentiating viral and bacterial infections; the results obtained indicate, however, that the ESR is an unreliable diagnostic criterion and that the final decision depends on other factors such as the clinical history, physical examination, the character of the spinal fluid, bacteriological findings, and course of the disease. One report[4] emphasizes the value of the sedimentation rate as a substitute for a lumbar puncture in "polio suspects." Of twenty-six suspected cases of poliomyelitis, fifty-seven per cent showed a normal ESR with normal cerebrospinal fluid; the possibility that some of these cases were abortive poliomyelitis could not be ruled out.

Frequently the problem arises of differentiating between poliomyelitis and other central nervous system infections in which the spinal fluid pleocytosis is mainly mononuclear. We have recently seen two patients who presented this very problem and in whom the final diagnosis was lead encephalitis and mumps meningoencephalitis respectively; in both the erythrocyte sedimentation rate was normal. Similarly, in one of two cases of proved tuberculous meningitis the ESR was within normal limits on admission to the hospital.

Bacterial meningitis usually produces an elevation of the erythrocyte sedimentation rate, but the rate may be normal in the acute phase in some cases, increasing only later in the disease. Usually the differential diagnosis between bacterial and viral infection of the nervous system is not too difficult, since the sugar determination and demonstration of bacteria in the spinal fluid substantiate the diagnosis. Of the twenty-two patients with bacterial meningitis observed in this report, fifteen had elevated erythrocyte sedimentation rates on admission to the hospital.

The ESR determinations in viral and postinfectious encephalitides observed during this study did not follow any predictable pattern and seemed to be somewhat similar to those observed in patients with poliomyelitis (See Table II). Epidemic parotitis is usually accompanied by a normal erythrocyte sedimentation rate and in those cases in which meningoencephalitis developed, no abnormality in the rate of fall of the erythrocytes was noted. The ESR in the encephalitides and meningitides due to other causes showed variable results (Table II).

It has been stressed[3, 4] that the sedimentation rate is of value in differentiating between rheumatic fever and poliomyelitis. Since the cerebrospinal fluid examination and sedimentation rate may be within normal limits in certain cases of rheumatic fever and poliomyelitis, it can easily be seen that one cannot rely on either of these determinations to make a diagnosis. Probably the most reliable method of making a diagnosis of either of these diseases, when in doubt, is to follow the course of the disease and rely on the clinical manifestations such as joint pains, heart findings, choreiform movements, paralyses, etc. It can easily

be seen that reliance on the sedimentation rate can be misleading in the differentiation of some cases of rheumatic fever and poliomyelitis.

The value of the erythrocyte sedimentation rate as a diagnostic tool in disease of the nervous system is limited. The results of this study indicate that this determination is of no value in determining the viral or bacterial etiology of neurologic infections in which there is spinal fluid pleocytosis. A thorough cytologic, chemical, and bacteriologic examination of the cerebrospinal fluid is indicated in all cases of suspected infection of the nervous system.

SUMMARY AND CONCLUSIONS

1. In uncomplicated poliomyelitis and other viral infections of the central nervous system the erythrocyte sedimentation rate is elevated in about 50 per cent of the cases at the beginning of the disease.

2. The erythrocyte sedimentation rate is unreliable in differentiating poliomyelitis from other infections of the central nervous system which simulate it.

3. No correlation could be established between the clinical type of poliomyelitis, the severity of the disease or the degree of abnormality of the spinal fluid, and the elevation of the sedimentation rate.

4. The differentiation of viral and bacterial neurologic infections cannot be made on the basis of the sedimentation rate value.

5. The erythrocyte sedimentation rate should never be used as a substitute for a diagnostic lumbar puncture.

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A PRELIMINARY REPORT ON RHEUMATIC FEVER IN VIRGINIA

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IT IS the purpose of this study to investigate the detailed circumstances of 225 cases of rheumatic fever seen in Virginia. Each of the patients has been followed at least three years or until death. We felt that the study of the race, sex, family history, preceding illness, season and age at time of onset of each attack, symptoms, physical signs, laboratory studies, and duration of each attack would lead to a clearer picture of the disease in this locality. The residual cardiac status of the patients, relationship of attacks to removal of tonsils and adenoids, average duration of the disease, and deaths have also been tabulated.

INTRODUCTION

The Virginia rheumatic fever program was initiated in May, 1940, administered under the State Crippled Children's Bureau, and operated on Federal funds. It was developed and has been maintained in accordance with the general policies outlined by the Children's Bureau Advisory Committee. This program has now been in operation seven and one-half years. Because relatively little has been known or written about the disease of rheumatic fever as seen in children in this state, we have, from the beginning, placed emphasis on careful and consistent history-taking and complete and repeated physical examinations. While it is realized that our period of observation is much too brief at this stage to point up anything in the way of prophylaxis, treatment, or ultimate prognosis, we do believe that a clearer picture of the disease, as it occurs in children in this southern state, is beginning to emerge. We, therefore, present our findings to date in this preliminary report.

As of June 1, 1947, a total of 1,205 patients had been seen in the Richmond clinic. Two hundred and twenty-five of these had been definitely diagnosed as having rheumatic fever and had been followed for at least three years. By a careful study of this latter group we have attempted to determine the similarities and differences between the disease here and in other geographic locations, which have been reported at length previously.[1]

It is well recognized that in such a protracted disease no final conclusions can be drawn in this relatively brief period of time. However, while the minimum period of known rheumatic fever duration was six months in two patients who died, only those living who were known to have had the disease for at least three years were included. The maximum duration was nineteen years, and the average, 5.95 years. Most of the patients (87 per cent) were seen here while the disease was active, but 13 per cent were referred for observation while the disease was inactive. All patients were under 21 years of age, as those exceeding this limit were referred elsewhere.

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It was felt that the period studied was adequate to fulfil one of our main purposes. This was, namely, to assist the practitioners in this section of the country in making an earlier diagnosis by a tabulation of the relative frequency of the cardinal early symptoms as seen here. While it will be shown that joint aches and pains in the extremities were among the most frequent early symptoms, many cases would be missed if acutely swollen joints were required for diagnosis. We found this condition in only 43 per cent of our cases. It used to be said that acute rheumatic fever was rare in Virginia, and yet old rheumatic heart disease was commonly recognized.

DIAGNOSIS

What then are the criteria for diagnosis? Leo Taran,[2] in his extensive studies with rheumatic children in New York, has written at length on the laboratory and clinical criteria of rheumatic carditis in children. We have, since the beginning of this clinic, followed approximately the same method of study in an attempt to arrive at a correct diagnosis and later to evaluate activity. The complete study included a careful history, physical examination with special attention to the heart, complete blood count, sickling preparation, urinalysis, stool examination, sedimentation rate, electrocardiogram, and x-ray or fluoroscopic examination. On the basis of these findings the patient was carefully considered. Only if at least one major manifestation, such as polyarthritis, carditis, chorea, old history of rheumatic fever, or nodules, was present with several of the minor ones, such as fever, rash, leg aches, abdominal pain, epistaxis, leucocytosis, elevated sedimentation rate, and anemia, was the diagnosis made.

In determining the duration of activity, Taran's ten points were emphasized. He weighs leucocytosis, anemia, sedimentation rate, pulse rate, fever, vital capacity, weight gain, A-V conduction, auscultatory evidence, and finally clinical observation as to fatigability and emotional stability. Emotional instability continued in 25 per cent when all other laboratory studies were normal. We are impressed frequently, as he was, that "the so-called quiescent interval might be considered as a form of mild rheumatic activity, presenting none of the classical and accepted criteria for rheumatic activity. . . The final decision as regards the presence or absence of active rheumatic disease rests upon clinical judgment. This, as in all other medical problems, is a product of continued and careful observation and examination of large numbers of children with rheumatic disease over the entire period of rheumatic activity and for years following the active episode."

DIFFERENTIAL DIAGNOSIS AND SELECTION OF CASES

As might be expected in a clinic designed for the diagnosis and treatment of rheumatic fever, in only about 40 per cent of the patients was that diagnosis made. No patients were seen except when referred by a physician as having suspected heart disease or rheumatic fever. Fig. 1 illustrates the distribution of cases. Of the 504 patients with rheumatic fever, 225 had had the disease at least three years or had died earlier, and this is the group on which the

detailed study of incidence and manifestations is based. The other 279 developed the disease after January, 1944, and will be studied later after the course of their illness has been followed for a longer period.

In 253, who are listed as being deferred cases, it was the opinion of the examining physicians that sufficient positive criteria for diagnosis had not been obtained for making a final judgment. This group is constantly being changed to one of the other categories. Later work should place most of them in some definite class.

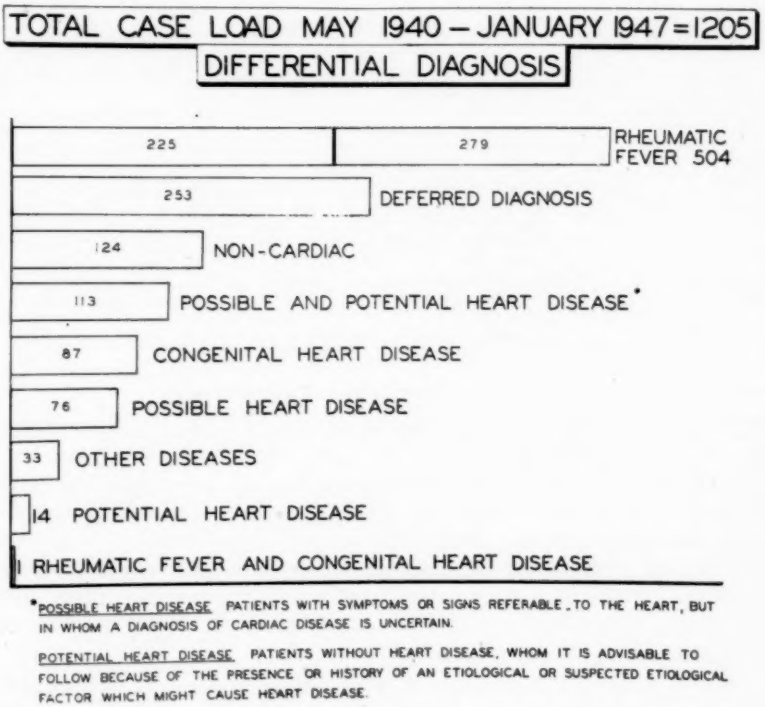
TOTAL CASE LOAD MAY 1940 – JANUARY 1947 = 1205
DIFFERENTIAL DIAGNOSIS
225
279
RHEUMATIC FEVER 504
253
DEFERRED DIAGNOSIS
124
NON-CARDIAC
113
POSSIBLE AND POTENTIAL HEART DISEASE*
87
CONGENITAL HEART DISEASE
76
POSSIBLE HEART DISEASE
33
OTHER DISEASES
14
POTENTIAL HEART DISEASE
1
RHEUMATIC FEVER AND CONGENITAL HEART DISEASE
*POSSIBLE HEART DISEASE. PATIENTS WITH SYMPTOMS OR SIGNS REFERABLE TO THE HEART, BUT IN WHOM A DIAGNOSIS OF CARDIAC DISEASE IS UNCERTAIN.
POTENTIAL HEART DISEASE. PATIENTS WITHOUT HEART DISEASE, WHOM IT IS ADVISABLE TO FOLLOW BECAUSE OF THE PRESENCE OR HISTORY OF AN ETIOLOGICAL OR SUSPECTED ETIOLOGICAL FACTOR WHICH MIGHT CAUSE HEART DISEASE.

Fig. 1.

The noncardiac patients comprised about 10 per cent of those referred to the clinic. There were 124 of these children in our total of 1,205.

"Possible and potential heart disease" was the diagnosis in about 9 per cent. As the American Heart Association classification indicates,[3] "possible heart disease" is the term used for patients who show abnormal signs or symptoms referable to the heart but in whom the diagnosis of heart disease is uncertain. "Potential heart disease" is reserved for patients without circulatory disease whom it is advisable to follow because of the presence or history of an etiological factor which might cause disease. As noted in Fig. 1, those with either possible or potential heart disease alone comprised a smaller group.

The patients with congenital heart disease made up 7.2 per cent of the total. One case was felt to be rheumatic fever superimposed on congenital heart disease.

Among the thirty-three other diagnoses, sickle cell anemia was the most frequent. This disease may so closely simulate rheumatic fever that routine sickle cell preparations are made on every new Negro patient admitted. Nephritis, rheumatoid arthritis, and tuberculosis were each seen in three or four cases. The remaining single cases are listed in Table I.

TABLE I. OTHER DIAGNOSES

DIAGNOSIS	NO. OF CASES
Sickle cell anemia	13
Nephritis	4
Rheumatoid arthritis	3
Tuberculosis	3
Ancyclostomiasis	1
Hyperthyroidism	1
Periarteritis nodosa	1
Acquired syphilis	1
Congenital syphilis	1
Lymphoblastoma	1
Hypothyroidism	1
Multiple myeloma	1
Leucemia	1
Infantile kidney	1

INCIDENCE: RACE, SEX, FAMILY HISTORY

In the City of Richmond the 1946 census gives a total population of 222,908, with 70 per cent white and 30 per cent Negro. The 37 per cent Negro patients in our group is, therefore, somewhat higher than the percentage of Negroes in the general population. Paul and others,[4] in their New Haven study, concluded that rheumatic fever is less common in Negroes but more virulent when it does attack. It is recognized that many more white patients than Negroes are treated by private physicians without referral to the central clinic. Ash,[5] in Philadelphia, found 83 per cent white and 17 per cent Negro with about equal division of white and Negro admissions.

The sexes were almost evenly divided, with 51.5 per cent females and 48.5 per cent males in our group. Coombs[6] found in his outpatient work in Bristol that almost two-thirds of his patients were females. Gibson[7] notes an incidence in girls of almost 2 to 1. Paul[8] observed that below the age of 13 girls are more often affected, while in adults men are. In over 1,500 patients Cohn and Lingg[9] found, as we did, that the sexes were affected in almost equal numbers. Fig. 2 illustrates our incidence figures.

In taking the history, an attempt was made to elicit the family history of (1) any heart disease, (2) rheumatic fever, (3) arthritis, or (4) allergy in the siblings, parents, uncles, aunts, or grandparents. Of the 225 in our series, fifty-two were aware of some type of heart disease, the specific type often not known. In thirty-nine cases (17.3 per cent) there was rheumatic fever in the family. Arthritis was reported in nineteen families, and allergy in eight others.

In Gibson's[7] series of 1,487 cases a rheumatic family history was obtained in 16.3 per cent, which varies only one per cent from our series. Histories are admittedly far from reliable, as parents remember little of their own illnesses and often have no medical attention for them. Other authors have found a much higher incidence, such as Coombs,[6] who obtained a positive family history in almost half of his cases. Wilson and Schweitzer[10] also found about one-half of their families to have positive histories. In the New Haven study, 21 per cent of Paul's[8] group of 122 families were rheumatic. They conclude that a rheumatic patient with negative parents has a 10 per cent chance of having rheumatic offspring. If a rheumatic child of a rheumatic parent is chosen, his chances of having rheumatic children are about 25 per cent.[4]

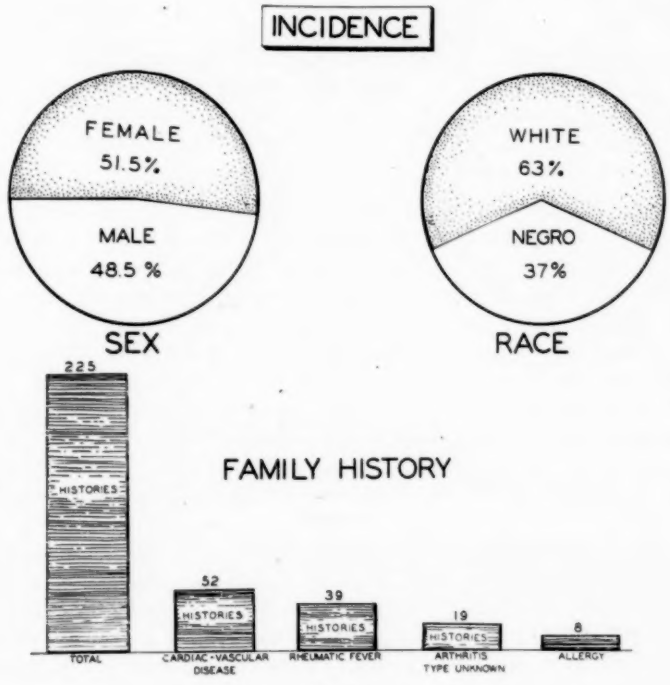

Fig. 2.

AGE

The Metropolitan Life Insurance Company's graph[11] based on Hedley's survey demonstrates the striking age susceptibility from 5 to 15 years. As Fig. 3 shows, we had a few patients in whom the onset occurred before 5 years of age. There is a sharp upward turn then, with a peak at 6 years. The significance of a second peak at 15 years is not clear. It is true that we did see a fair number of patients in their teens, but after 15 there is a sharp decline. Our average age

of onset was 7.87 years, which was very close to that found by others. Stroud[1] and Wilson and his associates[12] found it to be 7.3 years, while Paul[13] finds it to be 7 years. Coombs[6] gives a higher average age—namely, 10.2 years.

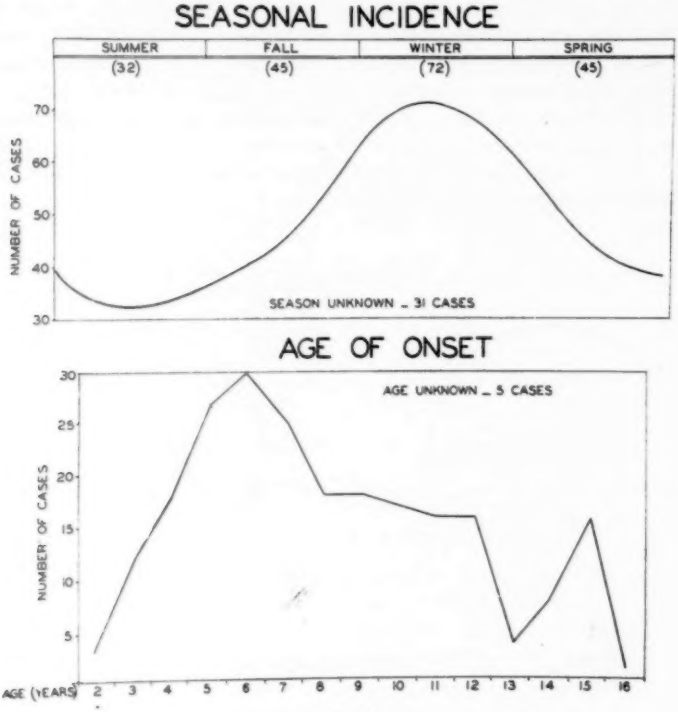

Fig. 3.

SEASON

The seasonal incidence was of special interest. Gibson,[7] in summarizing 1,135 attacks, both primary and recurrent, found a high point in April. This has been true for the country as a whole. The peak in our 225 cases was in January. The initial attacks occurred in the winter in seventy-three cases. Autumn and spring were about equally divided with forty-six and forty-eight cases respectively, with the lowest point in the summer (thirty-seven cases). Actually, November, December, and January were our months of highest incidence, with April and July being next, as Table II illustrates.

The season for second or later attacks was about the same. There were eighty-five in the winter, fifty-four in the spring, forty-two in the fall, and thirty-five in the summer. Again January was by far the most prominent single month.

All this is in keeping with the observation of Stroud and his associates[1] that the farther north you go, the later the high point. They say: "Coombs finds

the incidence maximal in England during the months of December and January; Levine finds the maximum in Boston during February; we find it maximal in Philadelphia during March; and the observations of Swift and Wilson suggest it may be maximal in New York later in the spring."

TABLE II. MONTH OF ONSET

MONTH	FIRST ATTACK	LATER ATTACKS
January	35	38
February	17	28
March	11	18
April	18	21
May	9	15
June	10	13
July	18	14
August	9	8
September	13	15
October	14	12
November	19	15
December	21	19
Unknown	31	20

ILLNESS PRECEDING INITIAL ATTACK

In looking for a clue as to the true etiology of rheumatic fever, much has been studied about the illness preceding the initial and subsequent episodes. In a few cases the preceding illness of the patients in our series was seen by our hospital staff, but in most instances it was necessary to rely on the history or the notes of the referring physician. That rheumatic fever often follows untreated cases of streptococcic sore throat with high antistreptolysin titers was shown by recent army reports.[14] There are volumes of evidence pointing to the relationship of rheumatic fever to the hemolytic streptococci, but reinfections by streptococci do not always reactivate the disease, even in patients with rheumatic heart disease.[8] The work summarized by Kuttner[15] on prophylactic sulfonamides in patients with inactive cases gives the striking agreement of seven

TABLE III. ILLNESS PRECEDING INITIAL ATTACK

ILLNESS		NO. CASES
Sore throat		98
Scarlet fever		9
Tonsillectomy		5
Other:		
Pneumonia	6	
Influenza	2	
Colds	2	
Measles	2	
G.C. vaginitis	2	
Chicken pox	2	
Burns	1	
Sinus infection	1	
Urinary infection	1	
Infectious hepatitis	1	
Pertussis	1	
Impetigo	1	
Nephritis	1	
Diphtheria	1	

clinics as to their value in prophylaxis. She concluded that this proved the importance of Group A beta hemolytic streptococci as a factor in the etiology. Jones and Massell[16] believe it is the volume of the streptococcal infection which is important rather than the particular type, from their studies on immune bodies and other phases of the disease.

Table III shows that in a little less than half of our patients a history was obtained of a sore throat or streptococcal infection preceding the onset of rheumatic fever. Nine cases of rheumatic fever were preceded by scarlet fever, six by pneumonia, and one each by a urinary or skin infection. Five occurred shortly after a tonsillectomy. Most of the other preceding illnesses were probably coincidental, but they are listed in Table III. Jones and Mote[17] found a cold or sore throat preceded the initial attack in 58 per cent of their series of cases, which agrees closely with our findings.

The history of tonsillectomy and adenoidectomy previous to the primary manifestations was found in thirty of 141 of the carefully studied patients of Stroud and his associates,[1] while ninety-two of the 141 developed symptoms before tonsillectomy and adenoidectomy were done.

Only 20 per cent of our patients had a tonsillectomy and adenoidectomy before the onset of the first episode. Thirty-three per cent had the operation after the disease was considered quiescent. In 47 per cent it has not been done.

Kaiser[18] and Mackie[19] show larger groups of cases, all of which suggest that first attacks of rheumatic manifestations occur from 34 to 50 per cent less often in tonsillectomized groups than in nontonsillectomized groups.

SYMPTOMS OF INITIAL ATTACK

Every effort has been made to elicit a true and complete picture of the symptoms of the first and later episodes by detailed history-taking. In the presence of any one of the cardinal manifestations of polyarthritis, carditis, chorea, or nodules, the diagnosis is clear. But the more elusive symptoms are found frequently to predominate in our series and call attention to an illness in which the carditis appears later. Joint pains head the list, as shown in Fig. 4, 157 of the 225 patients having joint pains in the initial attack. Fifty-nine patients experienced pain only, while 98 were acutely swollen. Sixty-eight showed no joint symptoms. One hundred and seven of our patients suffered aching of the extremities without joint involvement. Cohn and Lingg[9] recognized the problem which faces any clinician who sees suspected rheumatic fever: "As initial phenomenon for dating the onset of rheumatic fever the meaning of muscle and joint pains has often been called in question. How to be certain when they are significant is difficult." They found true polyarthritis in 40.3 per cent, and muscle and joint pains in 9 per cent of their series. Muscle pains are less impressive than joint aches, and the latter are considered significant only when additional evidence for a diagnosis is given. Wilson[20] found growing and joint pain in 26 per cent and polyarthritis in 22 per cent of her cases.

Fever was a dominant symptom occurring in 146 patients of our series. It is likely that had the patients all been observed more carefully it would have been seen even more frequently than the histories indicate.

The generalized symptoms of illness, such as malaise, fatigue, anorexia, pallor, irritability, and weight loss, were important in the parents' minds, as Fig. 4 indicates. Obviously, these are not diagnostic of rheumatic fever, but frequently were reasons for seeking medical attention in the absence of striking joint symptoms. The diagnosis was definite in sixty-eight of our patients in whom there was no joint involvement, with usually the more vague symptoms leading to the discovery of a carditis. Severe abdominal pains were noted in eighty-eight. Several were sent to the hospital as having suspected appendicitis.

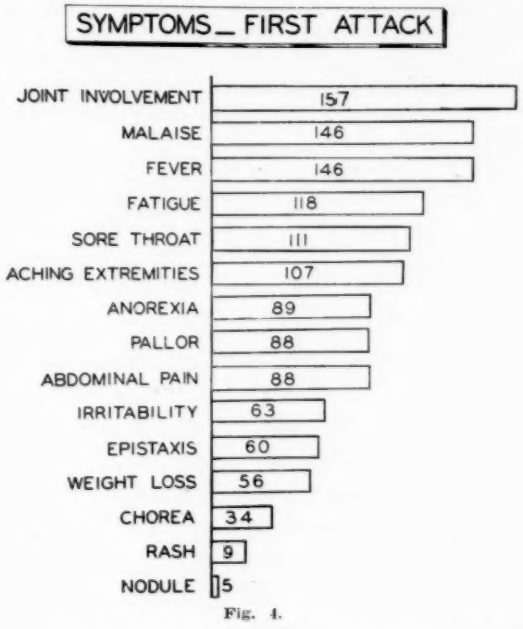

Fig. 4.

TABLE IV. SYMPTOMS DURING INITIAL ATTACK

SYMPTOMS	DURING FIRST MONTH ONLY	LASTING BEYOND FIRST MONTH OR STARTING AFTER FIRST MONTH
Fever	56	105
Malaise	31	103
Pallor	16	77
Anorexia	25	68
Weight loss	19	36
Irritability	7	57
Fatigue	26	102
Abdominal pain	51	66
Aching extremities	27	96
Joint involvement	64	91
Rash	9	10
Epistaxis	24	41
Sore throat	50	67
Chorea	7	29
Nodules	1	4

A sore throat was a definite symptom in 111 patients and was frequently recurrent. Epistaxis was a feature in sixty children. In 15.1 per cent, or 34 cases, chorea was seen as an initial manifestation. Wilson[20] found 23 per cent with chorea, and Cohn and Lingg[9] record only 9.9 per cent.

A history of a rheumatic rash was elicited in nineteen of our patients. Nodules were seen in only five, or 2.2 per cent.

Table IV represents an attempt to note any difference in symptoms between the first and later months of the initial attack. Almost all the symptoms persisted beyond the first month or became more evident in the second or later months. This is as might be expected with a disease of such a chronic nature.

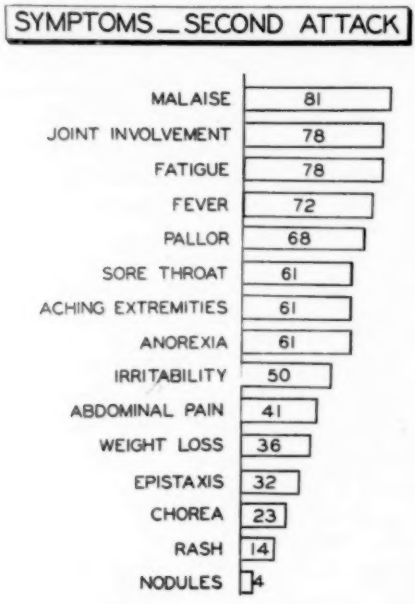

Fig. 5.

SYMPTOMS OF SECOND ATTACK

The symptoms of the second attack did not differ profoundly from those of the first (Fig. 5). Malaise and fatigue feature most prominently, but joint involvement was noted in seventy-eight of the 136 children who had more than one episode. Since eighty-nine of our patients had only a single attack, the total incidence of each symptom in the second attack is decreased proportionately. However, the relative order of frequency of sore throat, aching extremities, anorexia, abdominal pains, pallor, epistaxis, chorea, rash, and nodules is parallel.

In Wilson's[20] study of recurrences, which she noted in 85 per cent of 673 patients, growing and joint pains were seen in 26 per cent and true polyarthritis in 15 per cent. We found some joint symptoms in an even higher percentage, namely, 58 per cent. She noted chorea in 21 per cent and we, in 16 per cent.

LABORATORY FINDINGS

The laboratory findings have received varying degrees of emphasis. Ever since Schilling suggested that acute infections or exacerbations are reflected in the hemogram while latent infections are sometimes expressed better with the sedimentation reading, this latter has received special attention with rheumatic fever. Fig. 6 shows the relative incidence of a sedimentation rate over 10 mm. an hour, white blood count over 10,000 and hemoglobin below 70 per cent. The first column shows exactly 100 children in whom the sedimentation rate was over 10 mm. Only eleven patients showed no rise. In 114 children the initial rate was not known. This test was more helpful than the leucocyte count, which was known to be elevated above 10,000 in only forty-one cases or 18 per cent. In 50 per cent it was not known, and in 32 per cent it was under 10,000. Wilson's[20] figures suggest that the greatest degree of leucocytosis occurs with the acute carditis, while chorea, joint pains, etc., show a lower range.

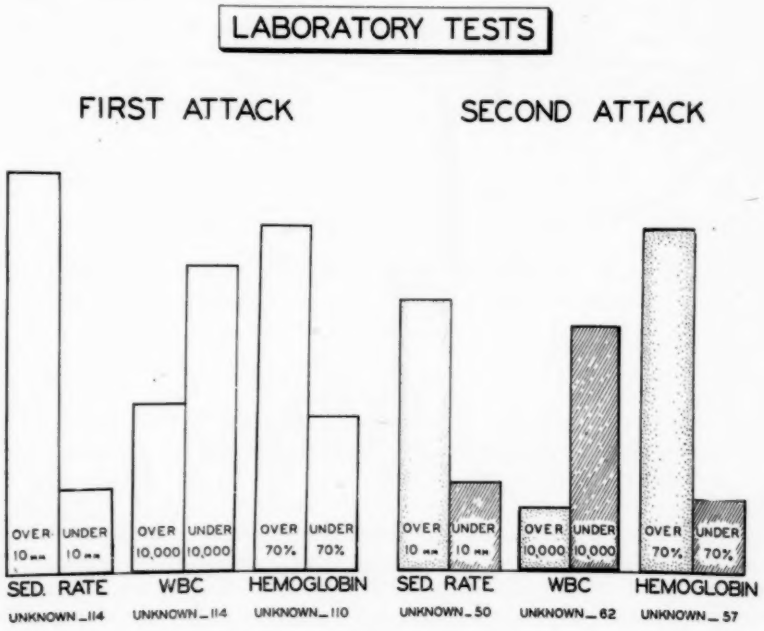

Fig. 6.

The secondary anemia which was often present during rheumatic activity is usually related to the severity and duration of the manifestation of the disease. Wilson[20] reported an average hemoglobin of 12 Gm. on patients admitted to the New York hospital. When seen by us, 18 per cent showed anemia with hemoglobin less than 70 per cent (15.6 Gm. standard). In about 50 per cent the hemoglobin was not known. Seventy-five children had no marked anemia.

The laboratory tests in second attacks of our series followed practically the same pattern with less striking leucocytosis and anemia.

NUMBER OF ATTACKS

During a period averaging eight years following the onset of the disease, 85 per cent of Wilson's[20] patients had one or more recurrences, whereas Cohn and Lingg[9] noted 75 per cent recurrences in their series of 3,129 cases. In both groups the greatest number of recurrences was between the ages of 5 and 14, and it was felt that puberty was of greatest importance in cessation of exacerbations.

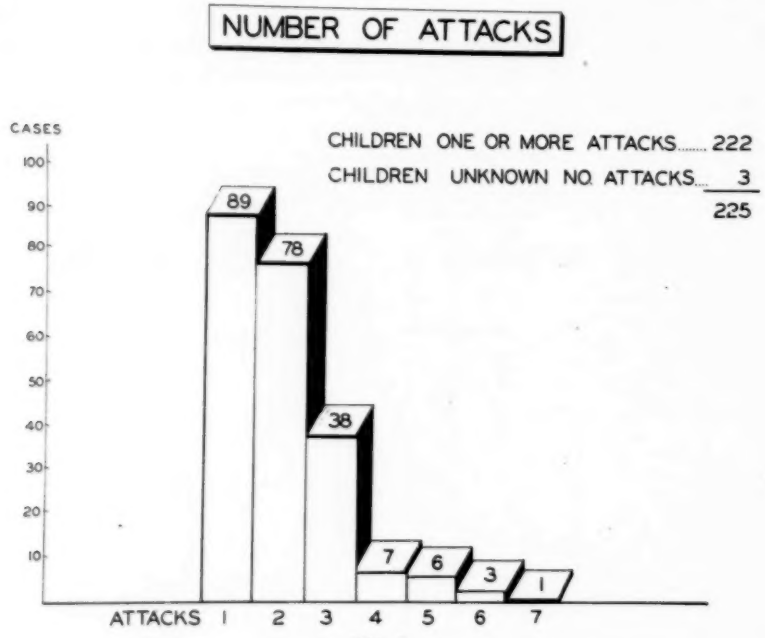

Fig. 7.

In our period of study, 61 per cent had recurrences. Of the 225 children, 39 per cent (eighty-nine) had one attack. Almost as many (seventy-eight) had two attacks and thirty-eight had three attacks. As shown in Fig. 7, there were seventeen patients who had more than three episodes. The patient who suffered seven attacks was followed in the Medical College of Virginia Hospital during each of these episodes.

TABLE V. COMPARISON OF RECURRENCES IN TWO SERIES

NO. ATTACKS	OUR SERIES %	COHN & LINGG[9] %
1	61	75
2	34	51
3	17	32
4	3	20
5 or more	4.4	12

The percentage of recurrences seen thus far in our series as compared with the series of Cohn and Lingg is given in Table V. In our series the recurrences will probably rise as the period of follow-up lengthens. Thus far, the average duration of the disease is 5.95 years.

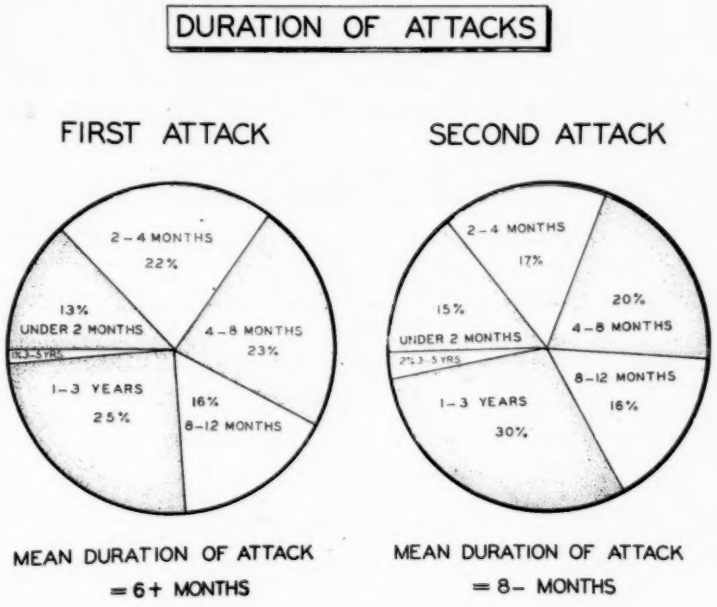

Fig. 8.

DURATION OF ATTACK

One of the most difficult quantities to measure in such a study is the duration of each episode of rheumatic fever. At each successive clinic visit, in addition to a history and physical examination, the usual laboratory and other tests suggested by Taran and others were repeated to attempt to gauge objectively the continuation of activity. Taran[2] estimates 25 per cent of his patients have continued activity which can be detected only by clinical judgment. In the opinion of the clinician in charge, the mean duration of the first attacks in our patients was just over six months. Fig. 8 illustrates the percentage in each group. In about 50 per cent the disease was inactive in six months. In 26 per cent the disease was active for more than one year.

For the second episode, the mean duration of attack was just under eight months. In about 50 per cent it lasted eight months, and in 32 per cent, longer than one year.

CARDIAC INVOLVEMENT

If it were not for the cardiac involvement in rheumatic fever, it would be considered in a class with other acute febrile illnesses and of little serious con-

sequence. But knowing that carditis in some form was found in all but four of Wilson's[20] 673 children and that Ash's[5] tabulation of a group of over 3,500 cases showed it in 60 to 79 per cent, we are forced to pay heed to suspicious preliminary symptoms. Cardiac involvement is used most often to refer to murmurs which were considered significant, abnormal sounds, enlargement or unusual contour of the heart, or electrocardiogram changes (Table VI). One or more of these abnormal factors was found in 188 or 83 per cent of our patients during the first or later attacks (Fig. 9). Of these 188 children, 132 showed changes during the original episode and fifty-six were added during later ones.

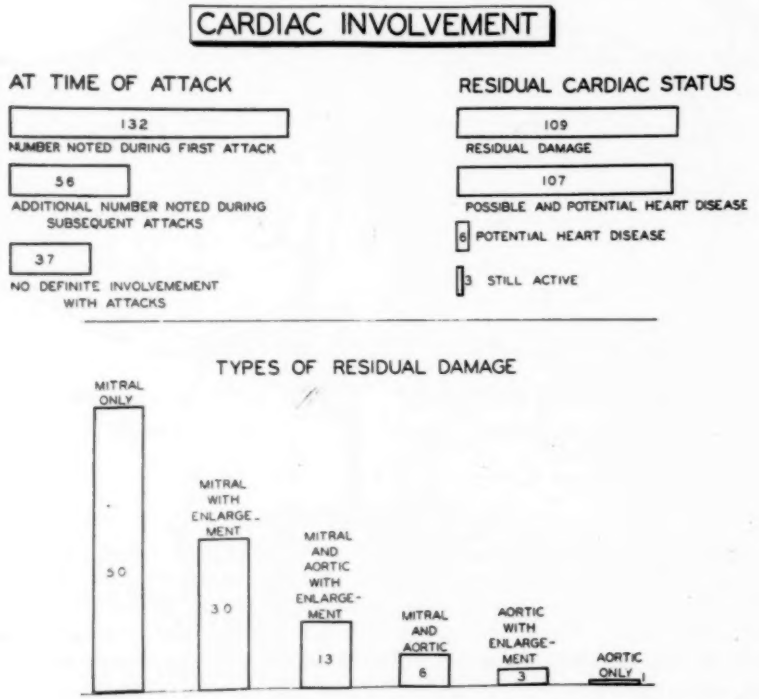

Fig. 9.

TABLE VI. HEART INVOLVEMENT IN INITIAL ATTACK

INVOLVEMENT	NO. OF CASES
Systolic murmur	107
Diastolic murmur	21
Abnormal sounds	44
Thrill	3
Enlargement of heart	40
Abnormal ECG	46
Abnormal cardiac contour	33
Cardiac failure	5
Friction rub	7

In thirty-seven cases, or 17 per cent, there was no definite evidence of carditis. Jones and Bland[21] found the incidence of heart disease to be 86 per cent in a series of 518 patients followed for eight years.

An evaluation of our 225 patients in repeated examinations revealed that of the 188 who had shown carditis with the exacerbations, 109, or 48 per cent of the total, showed residual cardiac damage. Fifty per cent are listed to date as having possible and/or potential heart disease, based on the American Heart Association's classification previously defined.

The types of residual damage are further elaborated at the bottom of Fig. 9. By far the greatest number are mitral lesions (eighty-five cases) with or without enlargement. Mitral and aortic insufficiency with enlargement comprised thirteen cases. Mitral and aortic insufficiency without enlargement totaled six cases. Single aortic lesions without mitral involvement were found in four cases.

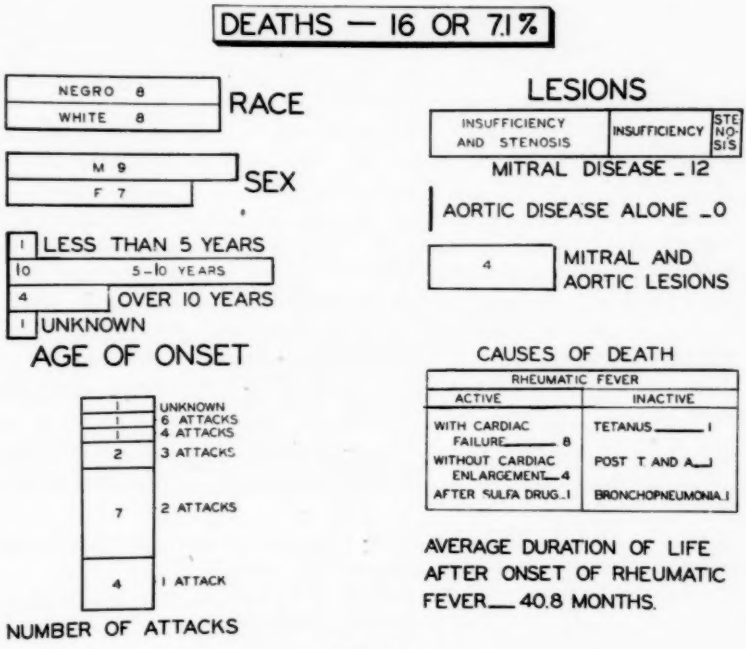

Fig. 10.

DEATHS

Our period of observation is admittedly insufficient for comparison with other figures as to death rates. Fig. 10 is presented solely to show the pertinent features of the disease as it occurred in sixteen children (7.1 per cent of our patients) who have died thus far. Similar to the series as a whole, these patients are about equally divided according to race and sex. The age of onset was 5 to 10 years in two-thirds of them. All but four had more than one attack.

Three-fourths of them had mitral disease, and one-fourth had both mitral and aortic involvement.

In three cases death could not be attributed directly to rheumatic fever. Tetanus, bronchopneumonia, and an anesthetic used with tonsillectomy and adenoidectomy were believed to be the responsible factors. In thirteen cases the disease was demonstrably active, and it was complicated by cardiac failure in 50 per cent.

The average duration of life in these sixteen children after the onset of rheumatic fever was just over three years.

It is interesting to note that in all but two cases there was a history of joint involvement. The other symptoms were not unlike those previously listed in order of frequency.

SUMMARY

1. Of a total of 1,205 patients referred by physicians to the Medical College of Virginia Rheumatic Fever Clinic from April, 1940, to June, 1947, as having probable rheumatic fever or heart disease, 504 had the diagnosis of rheumatic fever confirmed, while 203 were being followed as possible and/or potential heart disease, and 253 were still being listed as deferred.

2. Two hundred and twenty-five, or 44 per cent of the 504 patients, were the subjects of special study since they had been followed for at least three years or until death.

3. The study of this group of 225 patients brought out the following facts:

The average duration of the disease was 5.95 years as followed thus far.

The sexes were about evenly divided.

Race incidence closely paralleled the percentage distribution in population.

A family history of rheumatic fever was obtained in 17.3 per cent.

The average age of onset of initial manifestations was 7.97 years.

January was the peak month for onset in both the initial and recurrent episodes.

A history of preceding streptococcal infection was obtained in about 50 per cent of the children. Only 20 per cent had had tonsillectomies prior to the onset of the disease.

Joint pains led the list in frequency of symptoms occurring with initial and secondary attacks. Fever and malaise ran close seconds.

Laboratory findings as to elevation of sedimentation rate, leucocytosis, and anemia were somewhat helpful but far from conclusive.

Sixty-one per cent had one or more recurrent episodes while under observation.

As nearly as could be estimated, the mean duration of the first attack was 6.4 months, and that of the second was slightly under eight months.

Cardiac involvement was demonstrable in 83 per cent of all patients during the active stages of the disease. Only 49 per cent showed demonstrable residual cardiac damage, but the rest are still under observation as having possible and/or potential heart disease.

Seven and one-tenth per cent (sixteen patients) died during the period of observation. The average duration of life after onset of the disease in these children was 40.8 months.

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Case Reports

POLIOMYELITIS IN A THREE-WEEK-OLD INFANT

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THE rarity of poliomyelitis in infants under 6 months of age prompts the reporting of this case. A review of the English literature reveals the youngest patient with poliomyelitis on record to be in a 2-week-old infant in the 1907 New York epidemic.[8] More recently Biermann and Piszczek[3] reported a case of poliomyelitis contracted on the eleventh day of life with fatal termination on the sixty-seventh day. The infant had been exposed for ten minutes to its mother, who showed clinical signs of poliomyelitis on the first post-partum day and died three days thereafter. Hess and Levinson[8] report the disease occurring in a 4-month-old infant and diagnosed in the preparalytic stage. A 6-year-old sibling had been stricken with a case of fulminating poliomyelitis eight days prior to the onset in the infant. Recovery in the infant was without sequelae. Lubchenco and associates,[9] in a statistical study of the 120 cases occurring at the Children's Hospital, Denver, during 1943, found the youngest child attacked to be 4 months of age. Five cases of poliomyelitis in infants are found recorded in foreign literature.[1, 5, 7, 10, 12]

It is generally accepted that until about the sixth month of age infants possess a passive immunity to poliomyelitis similar to the immunity demonstrated to diphtheria. The foundation for this belief is the work of Aycock and Kramer[2] who showed that serum from the cord blood of ten out of twelve newborn infants possessed the same neutralization power to poliomyelitis virus as did the blood serum of their mothers.

The following report is of a case of meningopolioencephalitis in a 3-week-old infant.

CASE REPORT

Clinical Findings.—The patient, R. H., was born on Sept. 21, 1947, delivery being uneventful. On October 8 (seventeenth day of life), he began to cry continuously, developed a fever, and appeared to have difficulty in swallowing when fed. He became drowsy and unresponsive to all stimuli and on October 12 was admitted to the hospital where physical examination revealed a very lethargic child who responded only to light stimuli. Respirations were 65 per minute, with a pulse of 120 per minute and a temperature of 100.5° F. The body was completely flaccid; the gag reflex was absent, and an effort was made to suck on the tongue blade. The chest and heart were normal. Petechiae which blanched on pressure were noted over both lower extremities.

Laboratory Data.—The red blood cell count was 4.95 million cells per cubic millimeter of blood, and the white blood cell count was 12,550 cells per cubic millimeter of blood. The differential white blood cell count showed 57 per cent of the cells present to be polymorphonuclear neutrophiles with 35 per cent lymphocytes and 8 per cent monocytes. A lumbar puncture was productive of clear spinal fluid under normal pressure. The spinal fluid gave a 3 plus Pandy reaction and was found to contain many red blood cells and 15 white blood cells per cubic millimeter of spinal fluid. The carbon-dioxide combining power of the blood was 57 volumes per cent. The blood sugar was 102 mg. per cent; the nonprotein nitrogen was 65 mg. per cent and the creatinine 2.6 mg. per cent.

From the Departments of Laboratories and Pediatrics, Mount Sinai Hospital of Cleveland.

Course in the Hospital.—On admission the child was given penicillin and caffeine sodium benzoate and placed in an oxygen tent. Respirations soon became Cheyne-Stokes in character. The baby went rapidly downhill and died twenty-four hours after admission, four and one-half days after the onset of symptoms.

Postmortem Findings.—An autopsy was performed one and one-half hours after death. Unfortunately, permission was not obtained for removal of the entire spinal cord. The body was that of a well-developed and well-nourished white male infant weighing 3,630 Gm. and measuring 68 cm. crown-heel length. The lips and nail beds were cyanotic, but otherwise there was nothing of note on the external surface.

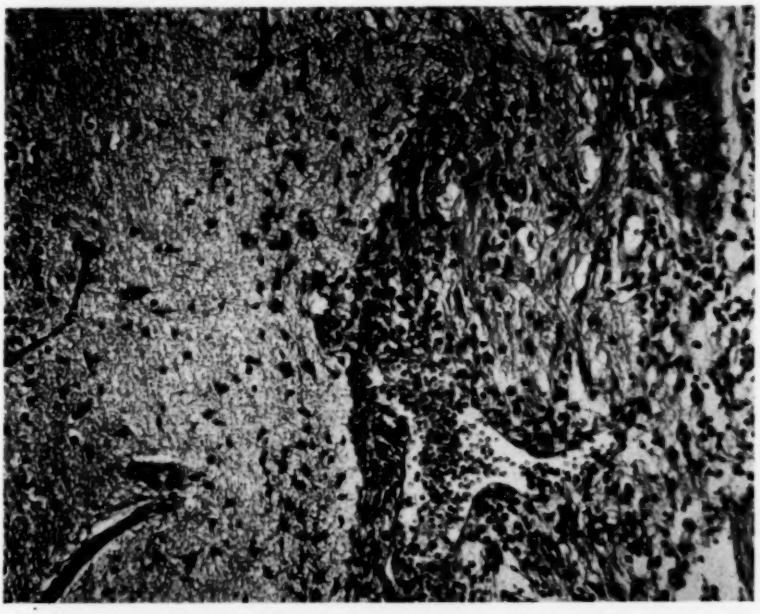

Fig. 1.—Section from the cerebral cortex showing infiltration of the meninges by lymphocytes and mononuclear cells.

Examination of the body cavities revealed the mesenteric lymph nodes to be moderately enlarged and the thymus pale and slightly edematous. Examination of the organs was essentially negative except for a partial pulmonary atelectasis.

There was slight prominence of the parietal bosses; the fontanelles were neither tense nor depressed. The brain weighed 560 grams (average normal weight, 380 grams). The meninges were smooth and glistening. There was moderate cerebral edema present with slight flattening of the gyri. The subarachnoid vessels were injected to a moderate degree. On sectioning the brain, the tissue appeared paler than usual with little differentiation of grey and white matter. Edema was evidenced by compression of the ventricles. The small amount of cervical spinal cord which was taken with the brain showed nothing of note grossly.

Microscopic sections from the cerebrum showed the leptomeninges edematous and infiltrated by numerous lymphocytes, plasma cells, mononuclear cells, and

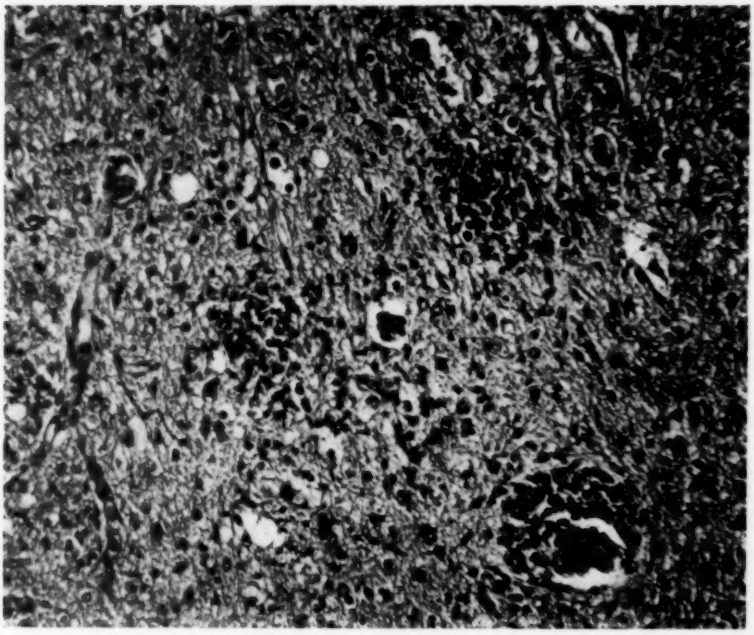

Fig. 2.—Section from the thalamus showing perivascular cuffing by lymphocytes and foci of inflammatory cells throughout the brain tissue.

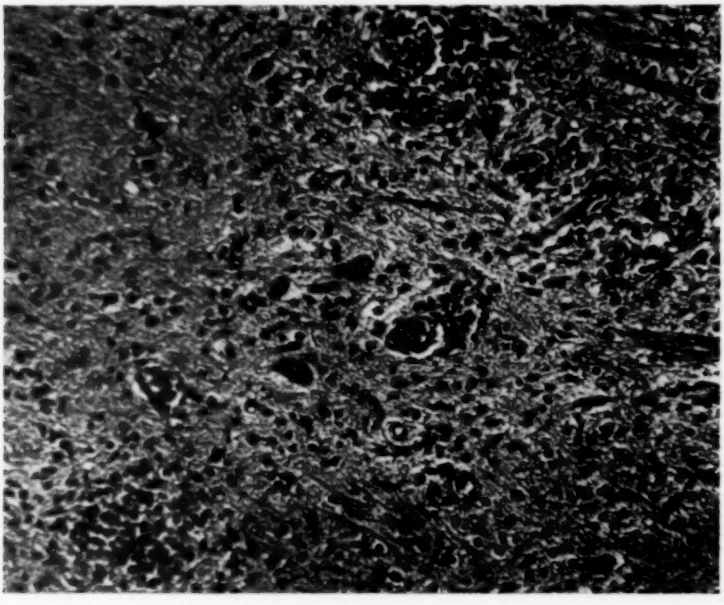

Fig. 3.—Section from the upper cervical spinal cord showing foci of lymphocytes similar to those seen in Fig. 2.

occasional polymorphonuclear neutrophiles. The subarachnoid vessels were engorged, as were the cerebral vessels. There was dilatation of the Virchow-Robin spaces with perivascular cuffing by lymphocytes (Fig. 1). Small foci of lymphocytes were scattered throughout the cerebrum, thalamus, and cerebellum (Fig. 2). Similar changes were found in the upper cervical spinal cord. Degeneration of the ganglion cells of the anterior horns was seen but without evident neuronophagia (Fig. 3).

Microscopic examination of lymph nodes removed from the mesentery showed the usual reactive phenomena of edema, vascular engorgement, and dilatation of sinuses with mobilization of mononuclear cells (Fig. 4).

Microscopic examination of all other tissues revealed nothing of significance except for cloudy swelling and fatty change of parenchymatous organs.

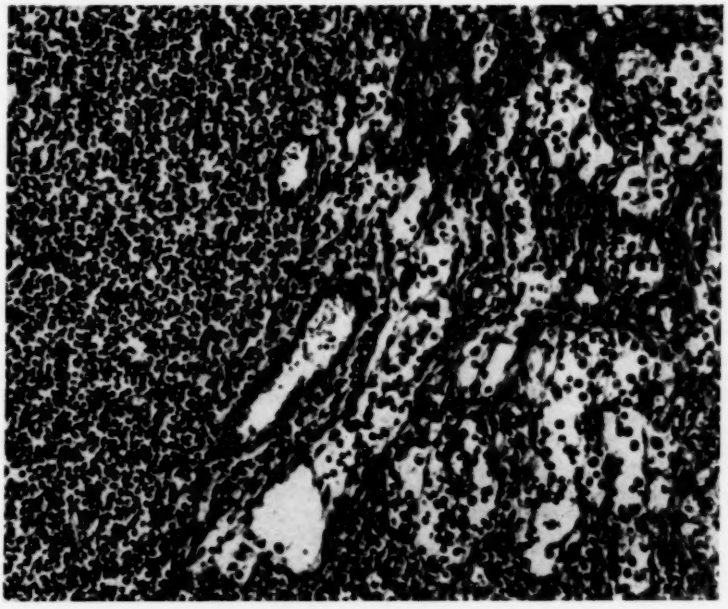

Fig. 4.—Section from a mesenteric lymph node showing marked dilatation of sinuses with moderate numbers of infiltrating monocytes present.

Discussion.—It was interesting to trace the probable source of infection in this case. Both the patient and his 4-year-old brother were exposed to a 13-month-old neighbor on Sept. 26, 1947. The neighbor became ill on September 29 and was hospitalized on October 1 at Lakewood Hospital where a diagnosis of poliomyelitis was made. He was transferred on October 6 to The Cleveland City Hospital where he died on October 14 after having spent the previous twenty-four hours in a respirator. Death was due to meningopolioencephalitis.

The patient's brother became ill on October 3 and on October 5 was diagnosed as having poliomyelitis by his physician who sent him to The Cleveland City Hospital where the diagnosis was confirmed. He suffered permanent residua of the disease with extensive involvement of the muscles of the trunk and lower extremities necessitating the use of braces and crutches for locomotion.

It is impossible to state whether the source of the disease in the patient was his brother or his neighbor, but probably the neighbor served as the common source of infection. A 2-year-old sister exposed to both brothers but not to the neighbor did not develop the disease.

Lubchenco[9] in the study of poliomyelitis at Children's Hospital, Denver, found multiple infections in nine families, with four cases in one family and three cases in another. It was noted that the first case occurring in each family was the most severe. Gebhardt and McKay[6] found forty-five cases occurring in twenty families, with thirty-two of the cases having a simultaneous onset or onset within five days after the other sibling developed poliomyelitis. These authors feel that in most instances multiple cases have their origin in a common source of infection.

SUMMARY

A fatal case of meningopolioencephalitis is reported in a 3-week-old infant whose older sibling likewise contracted the disease, both cases possibly having a common source of infection in a fatal case occurring in a neighbor. Four cases of poliomyelitis in infants under 6 months of age reported in the English literature are reviewed.

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HEMORRHAGIC SKIN MANIFESTATIONS ACCOMPANYING HEMOPHILUS INFLUENZAE MENINGITIS

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HEMORRHAGIC skin manifestations occurring during the course of *Hemophilus influenzae* meningitis are extremely rare. An extensive survey of the literature disclosed that only two such cases[1] have been previously reported; hence it was deemed of interest to report the following case.

CASE REPORT

R. C., a 6-year-old Negro boy, was admitted to the Children's Hospital Nov. 28, 1947, because of drowsiness, headache, and a rash on his abdomen. He had apparently been well until two days prior to admission when he developed a persistent frontal headache and vomited once. His mother ascribed this to constipation and administered a laxative and aspirin. The headache persisted, and during the morning of the day prior to admission he vomited two times, following which another laxative was given with poor returns. In the afternoon the mother noted that he cried out when touched or moved. Liniment was applied without relief. He refused all food that day and in the evening was unable to turn his head or bend his neck. Fever and mild delirium were noted at that time. He slept poorly during the night and on the morning of admission developed a "rash" on his abdomen and diplopia and became quite drowsy. There was no known exposure to contagion.

The past and family histories were irrelevant.

On admission to the hospital the temperature was 100.8° F., pulse 108, and respirations 25. The pupils reacted sluggishly to light, and no subconjunctival hemorrhages were noted. The fundi, ears, nose, and throat were clear, and the mucous membranes presented no hemorrhages. The lungs were clear to percussion and auscultation, and the heart revealed a sinus tachycardia with a rate of 108, P_2 greater than A_2, no enlargement and no murmurs. A few small, discrete, cervical and inguinal lymph nodes were palpable. The abdomen and genitalia were normal. A petechial rash was present over the abdomen, thorax, and upper extremities, no hemorrhages being noted on the palms, soles, lower extremities, or face. There was a marked stiffness of the neck, and the Kernig and Brudzinski tests were strongly positive. All deep tendon reflexes were hyperactive.

Spinal fluid obtained on admission was cloudy and was reported as follows: protein 600 mg. per 100 c.c., sugar 5 mg., and leucocytes 6,800, with polymorphonuclears 95 per cent. A rare gram-negative bacillus was found on direct smear, and from a culture, gram-negative pleomorphic bacilli morphologically and culturally resembling *H. influenzae* were obtained. Smear and culture of material aspirated from one of the petechiae showed gram-negative bacilli morphologically resembling *H. influenzae*. The blood culture grew *H. influenzae*. Following this report 50,000 units of streptomycin were instilled intrathecally, and 125 mg. of precipitable nitrogen anti-influenza Type B rabbit serum (with one gram of sulfadiazine) were given intravenously in 500 c.c. of 5 per cent glucose and Hartman's solution. Sodium sulfadiazine, one gram, was given orally every four hours with equal doses of sodium bicarbonate, and 200,000 units of streptomycin were injected intramuscularly every three hours.

The admission blood count was as follows: 9 Gm. per cent hemoglobin, 2.9 million red blood cells, and 9,000 leucocytes, with 85 per cent neutrophiles.

From the Children's Hospital, and the Department of Pediatrics, George Washington University School of Medicine.

On the second hospital day 50,000 units of streptomycin were again instilled intrathecally, and the spinal fluid at that time contained protein 300 mg., sugar 45 mg. and 3,900 leucocytes, of which 90 per cent were polymorphonuclears. The sulfadiazine blood level was 13 mg. The intramuscular streptomycin was reduced to 150,000 units every three hours and the oral sulfadiazine increased to 1.5 Gm. every four hours. The patient appeared much improved clinically and answered questions readily. The petechiae on the anterior trunk had regressed, but a new crop had appeared on the back. A culture of the moderately injected pharynx revealed nonhemolytic *Staphylococcus albus* and *Neisseria catarrhalis.*

Again on the third hospital day additional petechiae were noted on the chest and arms. On this same day a profuse nosebleed occurred, lasting for one and one-half hours and stopping spontaneously. A blood count at that time showed 40,000 thrombocytes, 7.5 Gm. hemoglobin, 3.0 million erythrocytes, and 5,250 leucocytes, with 46 per cent neutrophiles. The blood sulfadiazine level was 7 mg.; however, due to the low white blood cell count it was deemed inadvisable to increase the oral dose of sulfadiazine. Five hundred cubic centimeters of whole blood were given intravenously at that time.

Subsequent spinal taps performed on the fourth, sixth, eighth, and thirteenth hospital days revealed cell counts of 193, 120, 58, and 10, respectively, with a predominance of lymphocytes on the first three specimens. Fifty thousand units of streptomycin were instilled intrathecally at the time of each puncture. Culture of the spinal fluid obtained on the fifth and sixth hospital days revealed *H. influenzae;* no growth was obtained on the eighth and thirteenth hospital days.

The sulfadiazine blood level was maintained between 4 and 10.7 mg. from the third to the fourteenth hospital days, and no attempt to increase this dose was made because the white blood cell count varied from 3,400 to 6,500.

Another transfusion of 350 c.c. of whole blood was administered on the sixth hospital day after a moderately severe nosebleed occurred. At that time the hemoglobin was 7.5 Gm., and the red blood cell count was 2.4 million. Another transfusion was given on the eighth hospital day when the thrombocyte count was 98,000. After several days the red cell count and hemoglobin gradually returned to normal as did the thrombocyte count, and they remained so till the time of discharge. Spinal fluid examinations on the eighteenth and twenty-first hospital days revealed 20 and 10 cells, respectively, with normal sugar and protein content and negative smears and cultures.

Sulfadiazine was discontinued on the fourteenth hospital day and streptomycin stopped on the fifteenth hospital day.

During the first seven hospital days the temperature ranged from 99.2° to 100.8° F. (rectal), the pulse from 90 to 150, and the respirations from 20 to 30. From the seventh to the twenty-third hospital days the temperature ranged from 98° to 100° F. (rectal), the pulse from 80 to 100, and the respirations from 10 to 20.

Additional medication consisted of vitamins K and C and liver extract parenterally.

On the fourth hospital day a herpetic lesion developed at the right angle of the mouth, clearing readily by the eighth day with symptomatic therapy.

Additional laboratory findings revealed essentially negative urinalyses, a negative old tuberculin, a positive Schick, no sickling of the red blood cells in a twenty-four-hour smear, prothrombin time 93 per cent of normal, bleeding time 1 minute, 30 seconds, and coagulation time 3 minutes, 10 seconds. On the sixth hospital day the patient's serum failed to cause capsular swelling of the infectious organism.

The physical and neurological examinations were negative, as were the blood and spinal fluid on the twenty-third hospital day when the child was discharged. Two months after discharge a complete physical examination revealed no abnormalities.

DISCUSSION

This case of meningitis due to *H. influenzae* represents the first to be reported in which these organisms were isolated from a petechia and the third reported case of *H. influenzae* meningitis accompanied by hemorrhagic skin manifestations. There are also two more such cases of hemorrhagic skin phenomena associated with this type of meningitis in the files of the Children's Hospital (petechial smears were not obtained in either of those cases).

Although petechiae occurring during the course of *H. influenzae* meningitis are extremely rare, they do occur and might be expected to be even more frequent, inasmuch as a bacteremia and septicemia generally accompany this form of meningitis. The literature contains several reports of Waterhouse-Friderichsen syndrome[1, 2] due to *H. influenzae* bacteremia and septicemia. The picture of bacteremia, septicemia, hemorrhagic manifestations, meningitis, and Waterhouse-Friderichsen syndrome due to *H. influenzae* is not unlike that due to meningococci, the over-all picture in both being merely the result of a fulminating bacteremia.

The case just reported is also of additional interest inasmuch as no residual neurological findings were noted despite the coexistence of a bacteremia, septicemia, and meningitis.

The repeated bleeding tendencies may be explained on the basis of capillary thromboses and hemorrhages due to the lodgment of *H. influenzae* and possibly to the thrombocytopenia.

SUMMARY

1. An extensive review of the literature and of the files of Children's Hospital disclosed five cases of hemorrhagic skin manifestations associated with meningitis due to *H. influenzae*.

2. In the case reported, *H. influenzae* was isolated from an aspirated petechia. Aspirations were not performed in the other four cases.

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COMPLETE ATRIOVENTRICULAR BLOCK ASSOCIATED WITH PATENT INTERVENTRICULAR SEPTUM

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COMPLETE heart block coexisting with congenital heart disease is rare. The lesion is uncommon, even in cases of interventricular septal defects, with which it is associated most frequently, according to the majority of authors. Since Von Stark, in 1903, first called attention to congenital complete atrioventricular block, some eighty to ninety cases have been reported in the literature. Wenner,[11] in 1944, classified eighty-five cases as being authentic instances of congenital complete heart block, while Crawford,[3] summarizing the literature on the subject in 1947, recognized only about sixty. Crawford analyzed all cases of complete heart block in younger age groups and cited White's series of 10,000 cases at the Massachusetts General Hospital, in which the incidence of this lesion was 0.79 per cent. Again, seventy-two cases of complete atrioventricular block reported by Graybiel and White[5] included only four cases of congenital heart disease and two cases of possible congenital heart disease.

Criteria for diagnosis of complete heart block in congenital heart disease consist of:

1. Symptoms or signs of congenital heart disease,
2. Bradycardia,
3. Electrocardiographic evidence of A-V block,
4. Negative history for infectious disease capable of producing complete heart block.

Atrioventricular block rarely may produce symptoms of palpitation or a disagreeable sensation in the chest or precordium in the adult. Usually, no symptoms at all occur in the presence of uncomplicated complete heart block; especially is this so in the infant.

CASE REPORT

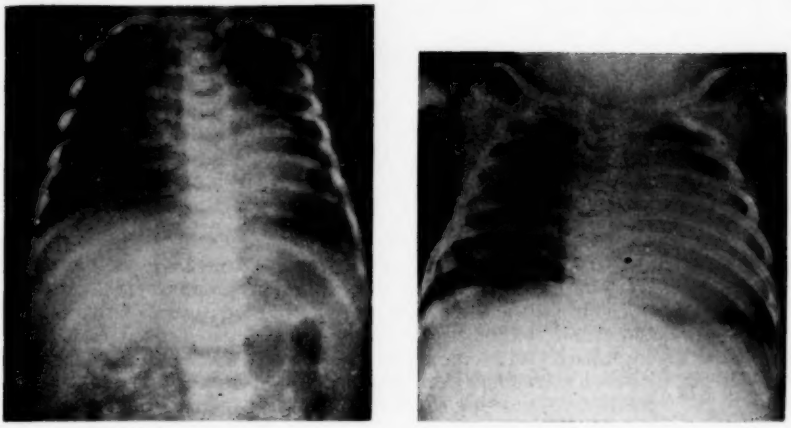
An infant girl was examined at the age of 5 weeks because of the presence of a very loud cardiac murmur. It was systolic in time, maximal between the third and fourth left interspaces, blowing in character, moderate in pitch, of grade 6 intensity, and transmitted slightly toward the left. A thrill was palpable.

The pulse was full, irregular, and with a maximal rate of 62 per minute.

Ante-partum examination of the mother had revealed the slow fetal heart rate. Post-partum examination of the infant revealed no other developmental abnormalities. The patient was the second child (the sibling being age 3) and was delivered uneventfully by the normal route. The mother was Rh negative, the father, Rh positive.

At birth, the child weighed 7 pounds, 14 ounces, but was difficult to resuscitate. At 5 weeks she had gained up to 8 pounds, 2 ounces, and at 8 weeks, to 9 pounds, 9 ounces, with an over-all height of 23 inches. She slept fitfully and during the day was extremely restless and irritable. No cyanosis was present. Feeding became an early problem. At 17 weeks the mother first noted intermittent slight cyanosis, especially when the child was asleep. No other changes occurred throughout this time.

From the Medical Service, Madigan General Hospital, Tacoma, Wash., Col. M. G. Keeler, M. C., Commanding; Lt. Col. J. P. Sullivan, M. C., Acting Chief of Medical Service; Major Massey, Chief of Cardiovascular Section.



A. *B.*

Fig. 1.—*A*, Roentgenogram of 5-week-old infant showing ovoid-shaped cardiac silhouette. Electrocardiographic tracings illustrate complete atrioventricular block (see Fig. 2). *B*, Roentgenogram of same infant at the age of 5 months. Note especially increase in cardiac size.

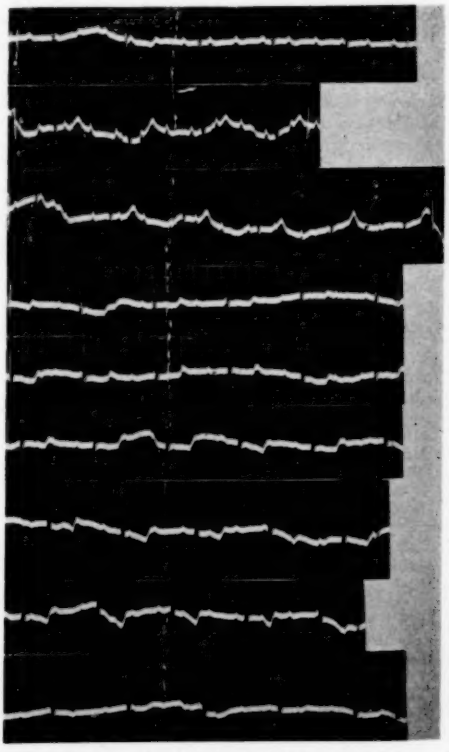


Fig. 2.—Electrocardiogram of 5-week-old infant, showing complete atrioventricular block.

The heart rate on physical examination varied from time to time as follows:

May 26, 1947	50 per min.
June 18, 1947	60 per min.
July 16, 1947	42 per min.
Aug. 7, 1947	62 per min.
Aug. 22, 1947	60 per min.
Sept. 17, 1947	54 per min.

On x-ray examination, at the age of 5 weeks, the cardiac silhouette was seen to be obliquely ovoid, but did not present a pathognomonic configuration. By the end of five months, the heart shadow almost completely obliterated the left hemithorax with prominence especially of the left ventricle. (See Fig. 1.) Fluoroscopic examination confirmed the impression of generalized cardiac enlargement with emphasis on left ventricular enlargement.

Electrocardiographic tracings were obtained at the ages of 5 weeks (Fig. 2), 5 months, and 7 months, all showing complete atrioventricular block.

On the basis of the clinical evidence, it is felt that the diagnosis is made correctly of a complete atrioventricular block associated with patent interventricular septum.

SUMMARY

A brief review of the literature on complete heart block coexisting with congenital heart disease is presented.

One case of complete atrioventricular block associated with patent interventricular septum diagnosed by clinical methods is presented, in view of the rarity of this lesion.

I would like to thank Dr. H. P. Thomas, Chester County Hospital, West Chester, Pa., for his kindness in referring this case.

Photographs courtesy of Alden Thoroughgood, M/Sgt., and the Madigan General Hospital Clinical Photographic Laboratory.

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MANDIBULAR FRACTURES IN CHILDREN

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GENERALLY speaking, fractures of the mandible in children present considerably more of a problem than they do in adults. The length and shape of the crowns of the deciduous molars make intermaxillary wiring somewhat impractical, plus the fact that varying stages of root absorption are usually taking place. The 6-year molars and permanent incisors, when present, usually have incomplete root formation and are not favorable for either traction or anchorage. In very young children, any method which would require the jaws to be firmly fixed together would not be desirable for obvious reasons.

The literature gives us very little help in the handling of these cases. A very recent and complete 1,500 page work on oral surgery[1] carries exactly seven lines on mandibular fractures in children. An excellent book on traumatic surgery of the jaws,[2] which devotes ninety-seven pages to the discussion of fractures of the mandible, fails to mention this problem as specifically applied to children. A very comprehensive synopsis of traumatic injuries of the face and jaws[3] also makes no mention of the problem. Peterson[4] reports treatment of a fractured mandible on a 5-year-old boy by means of an arch bar and intermaxillary tie wires.

Skeletal fixation, which has proved to be of great value in certain types of cases, is definitely contraindicated due to the danger of inserting pins in the tooth buds of the permanent teeth, which are very close to the inferior border of the mandible. In uncomplicated cases without much displacement of the fragments, a head cap with an elastic bandage under the chin will sometimes provide enough stability and fixation. In place of the plaster head cap, which is very heavy and uncomfortable on children, the canvas aviator-type of helmet, which we have all seen small boys wearing, is very effective. The wide ace elastic bandage can be fastened to each ear tab with a safety pin and tightened up from time to time by the child's mother. Fortunately union takes place very rapidly in cases without infection.

In cases where there is wide separation of the fragments and considerable traction is going to be required to reduce the fracture, plus very firm fixation to keep the fragments in apposition, open reduction and direct bone wiring appears to be the most logical treatment. Such a case is presented herewith.

CASE REPORT

History.—On April 19, 1948, a 6-year-old white boy living on a farm in Mississippi was riding with his father on a tractor pulling a disc plow. He fell from the tractor, and the plow passed over him. He sustained a severe 18-inch laceration along the inner surface of his left leg and thigh, a 2-inch laceration along the lower border of the right side of the mandible exposing the bone, a fracture of the head of the left tibia, and a fracture of the right side of the mandible between the first permanent molar and the second deciduous molar.

First Aid Treatment.—He was taken to a nearby hospital, where he was given tetanus antitoxin and the wounds cleaned and closed. A rubber dam drain was left in the wound of the jaw.

Clinical Examination.—The patient was brought to St. Vincent's Hospital, Birmingham in a car and was first seen about noon on the day after he was injured. His general condition was only fair. He had slept very little the

previous night (even though he had been given sedation) and was exhausted from the long trip in the car. There was no evidence of any brain injury. The mandible was markedly displaced forward and to the left giving the clinical appearance of a dislocation. He could not close his mouth and had been drooling saliva to such an extent that he was quite dehydrated. His father stated that he had been unable to take any fluids by mouth since the injury. The temperature was 101.2° F., the pulse rate 130.

Fig. 1.—Fracture of right side of mandible of 6-year-old boy with wide separation of fragments. Note radiolucency of the V at the front of the posterior fragment and the corresponding radiolucency in the anterior fragment which indicate the inner cortex is on one fragment and the outer on the other. The permanent molar in the posterior fragment should be up against the deciduous molar in the anterior fragment. The developing cuspid and bicuspids can be seen in the anterior fragment and the developing 12-year-old molar in the posterior fragment.

Roentgenographic Examination.—The roentgenogram of the right side of the mandible (Fig. 1) revealed a complete fracture just anterior to the first permanent molar, which had not yet erupted. There was such a wide separation of the fragments, due to the left and forward displacement of the anterior one, that the condition might have been misinterpreted as the loss of a tooth together with some bone substance. Upon closer examination, however, the two deciduous molars were seen to be present in the anterior fragment and the first permanent molar and developing crown of the second permanent molar in the posterior fragment. The third molar is, of course, not present at this age.

The radiolucency of the V on the anterior border of the posterior fragment and that of the corresponding V on the anterior fragment indicated that the inner cortex was present on one and the outer on the other.

The roentgenogram of the left side of the mandible revealed no evidence of fracture.

Laboratory Examination.—R.B.C., 3,150,000; W.B.C., 11,000; differential, 77 polymorphonuclears, 18 lymphocytes, 5 large monocytes; hemoglobin, 57. Urine: negative.

Treatment.—The patient was given tetanus and gas gangrene antitoxin on admission and also 500 c.c. of 5 per cent glucose in normal saline, intravenously. Penicillin, 50,000 units every three hours, was started. He was given $\frac{1}{300}$ gr. of atropine at 3 P.M. and taken to the operating room at 4 P.M. for open reduction of his fractured mandible.

Fig. 2.—Postoperative roentgenogram showing perfect reduction and fixation with tantalum wire. The horizontal loop goes through a hole in the lower border of each fragment. The vertical loop goes through a hole in the center of the V in the posterior fragment and corresponding hole in the center of the V in the anterior fragment. The two ends of this loop have been twisted together under the lower border. The developing teeth have been carefully avoided. The vertical loop gives the appearance of being in the second bicuspid follicle, but this is caused by angulation as the hole is beneath it.

Operation.—Under ether anesthesia an incision was made beneath the lower border of the mandible which incorporated the original wound. The ends of the bone fragments were exposed and easily approximated after cleaning out the interposed soft tissue. Using the smallest drill available and drilling slowly to avoid heat, a hole was placed in the middle of the V on the posterior fragment and one in the corresponding spot in the anterior fragment so that when the fracture was reduced these holes coincided. As was thought from study of the roentgenogram, the hole in the posterior fragment had to go through only the outer cortex and that in the anterior fragment through the inner cortex. A piece of tantalum wire, 0.020 of an inch in diameter, was placed through these two holes and tightened under the lower border of the mandible. A hole was then drilled in the lower border of each fragment about one centimeter from the fracture line, extreme care being taken to get beneath the tooth buds of the developing bicuspids. Another piece of 0.020 tantalum wire was placed through these holes and twisted together. The mandible was now very firm and stabile. The anesthetist reported that the teeth now came together perfectly and also remarked on the improvement in the patient's respiration upon reduction of

the fracture. There was no evidence of bleeding into the mouth. The subcutaneous tissues were closed with 00 catgut and the skin with black silk. The immediate postoperative condition of the patient was good. He was given 500 c.c. of 5 per cent glucose in normal saline during the operation. A cast was applied to the left leg and a window made in the cast so that the soft tissue wound could be dressed.

Course.—The postoperative course was surprisingly smooth and uneventful. He was given ¼ gr. codeine by hypodermic injection upon return from the operating room. After reacting from the anesthetic he began to take fluids by mouth for the first time since injury. The temperature at 8 P.M. was 102.4° F. He had a very good night, and the temperature the following morning was 99.6° F. There was very little pain or swelling, and he could swallow freely. He was given 500 c.c. of whole blood and 500 c.c. of normal saline. Fluids were given freely by mouth. The postoperative roentgenogram (Fig. 2) showed the fragments to be in perfect position.

On the second postoperative day his temperature was 99.4° F. There was no pain and very little swelling of the jaw. Half of the skin sutures were removed.

On the third postoperative day he was returned home to be placed under the care of the referring physician. Before leaving the hospital he was given 300,000 units of Duracillin.* His temperature was normal, and his general condition was very good.

The remainder of the skin sutures were removed by his physician one week later, and he reported that the wound had healed perfectly with no evidence of drainage or infection. The patient was on a soft diet and the jaw functioning perfectly with no discomfort. Subsequent reports indicate that firm union has taken place with no evidence of tissue irritation from the tantalum wires.

SUMMARY

1. Fractures of the mandible in children present difficult and individual problems quite different from similar cases in adults.

2. The literature contains very little reference to these cases.

3. In complicated cases open reduction appears to be the method of choice, but extreme care must be exercised to avoid the permanent tooth buds.

4. Tantalum wire, as first reported by Burch and Carney[5, 6] and later by Bellinger,[7] causes less foreign body reaction than any other material that has been used thus far.

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*Made by Eli Lilly and Company, Indianapolis, Ind.

Medical Care

COMMON RESPIRATORY TRACT INFECTIONS IN INFANTS AND CHILDREN

Diagnosis and Treatment

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ALTHOUGH important advances have been made in our knowledge regarding certain of the respiratory diseases, the great majority of these common infections still defy accurate classification. Terms such as nasal pharyngitis, bronchitis, and "flu" are almost meaningless as applied to describe these infections. Applying such terms to respiratory tract infections is comparable to speaking of the inflammatory diseases of the meninges as spinal or cerebral meningitis. The intelligent management of the various forms of meningitis today requires an accurate etiological diagnosis. Unfortunately, we do not as yet have many practical laboratory methods for the diagnosis of respiratory tract infections, but we do have a greatly improved understanding of the pathogenesis and etiology of these diseases. By approaching respiratory tract infections etiologically we should improve our ability to recognize them.

Infants and children who are being attacked for the first time offer an opportunity to study the clinical and pathologic features of these varied diseases in their relatively pure form. It seems important to conceive of the respiratory tree as a single unit which is capable of extremely varied reactions to infectious agents. These reactions may take various forms in the human subject, dependent upon age, immunologic, physiologic, and many other factors, such as dose, which serve to alter the picture. Different agents may produce a similar clinical picture and a single agent such as influenza A may simulate any stage of respiratory disease from latent or mild to extremely severe respiratory tract involvement. Dingle[1] has recently pointed out that the undifferentiated respiratory tract infections can be segregated "only by the exclusion of diseases of known cause, such as tuberculosis, diphtheria, beta hemolytic streptococcus infections, influenza, and psittacosis." Additional common diseases such as measles (rubeola), scarlet fever, and whooping cough might be added to this list.

The problem of the largest group of undifferentiated respiratory diseases still remains; and, as Dingle[1] states, they form a "clinical spectrum" extending from the common cold to atypical pneumonia. The Commission on Acute Respiratory Diseases has been able to separate four etiologic groups which clinically may fuse with one another, but still have different etiologic agents (most probably viruses) and certain definitive features when studied critically. The four categories which may represent separate etiologic entities are as follows:

1. The "common cold."
2. "Acute respiratory disease" (ARD).
3. Nonbacterial exudative pharyngitis and tonsillitis.
4. Primary atypical pneumonia.

Many previous workers[2-5] have demonstrated that the coryzal type of cold with a one- to two-day incubation period could be transmitted to well human beings by bacteria-free filtrates, but the Commission on Acute Respiratory Diseases[6] deserves the credit for delineating a second type of mild respiratory disease which is a separate and distinct entity most probably due to a virus. This disease they have chosen to call "acute respiratory disease" (ARD). It is distinguished by a five- to six-day incubation period, feverishness, chilliness, and headache. Sore throat is common but of rather mild degree in comparison to the patients who have exudate in the throat. This disease has been transmitted to human subjects by bacteria-free filtrates, and has been shown to be immunologically distinct from coryza-type colds. Rechallenge of subjects showed complete protection to this agent whereas no protection on rechallenge was demonstrated in subjects who had previously been infected with coryza-type filtrate. No cross immunity could be shown, which served further to define these agents as separate and distinct.

In infants and children the same "clinical spectrum" applies but may be more sharply defined in many instances. The first colds of normal full-term babies usually appear in the first few months as mild, almost afebrile coryzal-type infections, characterized by sneezing, cough, and "stuffed-up" noses. There may be mild anorexia. The physical findings are minimal and the white blood count is usually normal. Acute respiratory disease is difficult to delineate sharply in the present state of our knowledge but these more febrile responses are usually not seen until later in infancy when they may be associated with complications of a secondary character such as otitis media or cervical adenitis. Bacterial pneumonias also may frequently be associated with this illness. A separate and distinct entity is seen early in infancy which we have chosen to call "primary pneumonitis of infancy." Further details of this disease will be given briefly in a later part of this paper.

Nonbacterial exudative tonsillitis and pharyngitis is described by Dingle[1] as "a mild disease of short duration. The onset is ordinarily gradual, and the early complaints of the majority of patients are those of feverishness, headache, and anorexia. Symptoms of sore throat, hoarseness, and cough, often productive, are noted by 75 per cent or more of the patients. . . Nasal symptoms are not prominent." Moderate injection of the pharynx with gray or yellow pin-head exudate on swollen lymphoid follicles is seen on examination of these patients. This disease is rarely seen in the early months of infancy but makes its appearance at about one year of age, at which time it is usually featured by a severe illness with an acute onset, and high fever, sometimes ushered in by a convulsion. The findings are those of moderate swelling of the pharyngeal lymphoid tissues with a gray or whitish exudate which tends to remain discrete. The exudate may not appear for twelve to eighteen hours after the rather dramatic onset in many of these patients. The disease runs a self-limited course in three or four days and complications are rare.

Exudative tonsillitis and pharyngitis due to beta hemolytic streptococcus is also an acute disease in childhood and can frequently be differentiated from the nonbacterial group by the physical findings. The membrane is dirty gray

or yellowish and often confluent, there is more edema and redness, and usually an associated cervical adenitis. Throat cultures reveal large numbers of beta hemolytic streptococcus as the predominant organism. The white blood count is elevated as a rule with an increase in polymorphonuclear cells. The final proof of invasion in these patients is dependent upon a definite change in the antistreptolysin titer, but this test has very little practical value. It should be remembered that the majority of cases of exudative tonsillitis are not due to beta hemolytic streptococcus and the patients will recover spontaneously. Patients who are severely ill with this disease and have large numbers of these organisms in their cultures should be treated with penicillin.

Primary atypical pneumonia as seen in childhood varies very little from the adult disease, except that it may be milder in the usual case. Many children have no complaints except for cough and some anorexia. If a roentgenogram of the lungs is taken, one is frequently startled by the infiltration which is usually light and patchy in character but may be limited to a definite area.

The diagnosis involves ruling out other diseases such as tuberculosis, bacterial pneumonia, psittacosis, Q fever, and influenza. The cold hemagglutination test is helpful when it is positive, but a negative test does not rule out the disease.

In infancy, primary pneumonitis[7, 8] may occur as an epidemic disease involving groups of babies in an institution, or occasionally it is seen to occur sporadically.[9] In the epidemics *all* stages of respiratory tract involvement occurred in the various patients in the same ward. Some of the babies manifested sneezing and cough *only*, others had marked cough with inspiratory dyspnea, while the majority were severely ill with attacks of cyanosis and marked dyspnea. In the sporadic cases which we have observed, the same symptom pattern of cough, dyspnea, and cyanosis has been manifested in the most acutely ill patients with pneumonitis. However, patients with mild cases with little or no evidence of lower respiratory tract infection have been seen. The age and maturity of the patient appear to be responsible in the main for the variations which are met. In the epidemics the morbidity and mortality have been extremely high in prematurely born babies as contrasted to normal full-term infants.

The onset of the illness in the baby is rather abrupt and at times the pulmonary symptoms may be the first observed. Sneezing and cough are the first symptoms in most of the patients. The temperature response is usually slight but may rise to 102° or 103° F. for a short time. There are few physical findings in the milder cases. The mucus in the pharynx is abundant, whitish, thick, and tenacious in character. Râles may be heard over the lung fields on careful examination. The roentgenogram of the lungs reveals diffuse shadows which are bronchial in distribution and usually widespread, but may be confined to a single lobe of the lung.

The diagnosis is made by the symptom pattern and by the rather characteristic shadows seen in the roentgenograms of the lungs. The white blood count is usually normal or only slightly elevated with an increase of lymphocytes.

Pharyngeal smears made from these patients in the acute stage of the disease reveal a great predominance of epithelial cells which contain typical cytoplasmic inclusion bodies. This finding is considered helpful in the diagnosis, particularly when the inclusion bodies occur in large numbers (10 to 20 per 100 cells) in patients who satisfy the other criteria of primary pneumonitis.

Many post-mortem studies have revealed a distinct pathologic picture in the lungs of infants dying from the epidemic form of this disease. The prominent features are destruction and proliferation of bronchial epithelium with peribronchial infiltration of mononuclear cells. Typical cytoplasmic inclusion bodies are found in the epithelial structures of the pulmonary tree. This includes the nasal, pharyngeal, tracheal, bronchial and alveolar tissues. Because of the probably ubiquity of this agent, the interpretation of the finding of inclusion bodies must be made with caution. The same point of view must be assumed as we now have regarding the beta hemolytic streptococcus. The finding of this organism in the nose or throat does not always mean that the patient is suffering from invasion by the coccus. Likewise the finding of inclusion bodies may or may not be significant. It seems to depend in the main on the correlation of this finding with clinical evidence of a characteristic disease, and whether they are found in large numbers exclusive of other findings in carefully prepared pharyngeal smear biopsies. The age of the patient probably plays a large role also in the occurrence of these bodies.

Influenza is an epidemic virus disease, highly communicable, which primarily affects the respiratory passages. Epidemics of influenza A are now established as occurring at fairly regular intervals of two or three years, usually beginning in the late fall or winter months. The last few epidemics of influenza B have occurred at approximately four-year intervals. It is important to recognize this fact as the diagnosis of influenza should probably not be made except during an epidemic. Its sporadic incidence is known to be rare.

In a study of an epidemic of influenza[10] occurring in infants and children, the disease was characterized by high, irregular, and biphasic fever curves. Leucopenia was not found to be present. Acute pharyngitis, often hyperemic, and lassitude were the most prominent physical findings. None of the patients manifested severe laryngitis or croup.

Influenza A virus was isolated from throat washings taken from a number of the patients and inoculated intra-allantoically into developing chick embryos. The serologic diagnosis of the epidemic was established by the demonstration of significant increases in neutralizing antibodies by means of the hemagglutinin inhibition test. The neutralzing antibody response of infants, who in all probability were having their first infection with influenza A virus, was found to be of approximately the same magnitude as that of older children.

In the serums of five infants who experienced their first known attack of influenza A, antibody response as measured by the agglutination inhibition test was greatest to the strain of influenza virus isolated from the nasopharynx of one of the infants. Mean antibody levels attained were progressively lower to the PR8 and W.S. strains of influenza A virus and swine influenza virus, respectively, although some antibody was formed against all of the viruses tested.[11]

The most characteristic clinicopathologic feature of epidemic influenza as seen in a recent proved epidemic was an acute pharyngitis.[12] The pharyngeal smears of over 300 young adults and children suffering from influenzal A infection were studied, as well as similar tissues from control groups during, and six months after the epidemic. Increased destruction of pharyngeal epithelial tissues was definite as compared with the control specimens. The single most important micropathologic feature of the pharyngeal exudate of these influenza patients was a mononuclear exudate, which is consistent with the pathologic findings in certain other types of virus infections, both in man and animals. In our study a polymorphonuclear exudate frequently presaged a complicating secondary bacterial infection.

TREATMENT

The intelligent management of the common respiratory tract diseases is dependent upon a reasonably accurate diagnosis. Inasmuch as the great majority of these infections can now be considered to be caused by nonbacterial agents, no specific drug therapy can be offered for the primary diseases. The occurrence of secondary or synergistic bacterial disease may offer a real indication for a specific drug, but our choice should be dependent on some accurate knowledge of the infecting organism.

In the patient with exudative tonsillitis and pharyngitis due to beta hemolytic streptococcus, full therapeutic doses of penicillin should be employed. In infants, we use doses of 50,000 to 100,000 units of aqueous penicillin given intramuscularly at twelve-hour intervals; sulfonamide drugs such as sulfadiazine are also effective and may be more practical and economical in the home treatment of patients. Doses of approximately one grain per pound of body weight are used in infants and small children, divided over the twenty-four hour day and given at four-hour intervals. Somewhat smaller doses are used in older children. A good intake of fluids should be encouraged when the patient is on sulfonamide drug therapy.

The most important consideration in the common respiratory tract infections should be directed toward prevention. Isolation of the premature and newborn infant is effective against these highly contagious diseases. Home life as opposed to institutional life is most desirable as a practical preventive measure. Most of the diseases are self-limited infections, and require no special measures over and above good hygiene and common sense, but complications are frequent and should be watched for and prevented whenever possible. It would appear to be a well-established fact that the common primary virus diseases are precursors of bacterial infections; thus, every effort should be employed which will aid in their prevention.

Congestion and irritation which lead to various degrees of pulmonary obstruction should not be underestimated as important factors leading to complications. Any means available for reducing the irritation, congestion, and obstruction should be helpful. Postural drainage has been used successfully, especially in infants where the passages are small and the infant may be physiologically unable to cope with the secretions and congestion caused by the primary infections. The upper as well as the lower pulmonary passages can be drained much

more effectively when infants and children are placed in the prone or abdominal position. Ineffective and troublesome cough is often markedly relieved by the use of posture alone. The cough is probably one of the body's most effective defense mechanisms and should not be suppressed unless it is beginning to interfere seriously with the patient's rest. The two primary diseases where some relief of cough is most indicated are measles (rubeola) and whooping cough (pertussis).

Aspiration or gravitation of infected exudate into the lung has been shown to be the main mechanism involved in the pathogenesis of bacterial pneumonia. In so far as posture may plan a role in preventing aspiration or gravitation, it should be helpful in the prevention of this serious complication of common respiratory disease.

Specific polyvalent vaccines have been shown to be effective in the prevention of type-specific pneumococcic infections. Their use in civilian practice has not as yet become widespread.

Vaccination against influenza A and B is the only method now in practical use for the prevention of primary virus diseases of the respiratory tract. It is effective only against influenza A and B and probably has no prophylactic effect against other virus diseases. The reactions are relatively mild when the proper doses are used. Infants under 6 months of age need not be vaccinated. Up to 2 years of age, .25 c.c. of vaccine is given subcutaneously in one inoculation only. From 2 to 6 years of age 0.5 c.c. is recommended, and from 6 years on, one c.c. doses are well tolerated. The present vaccines should not be given to egg-sensitive children. One inoculation would appear to be about as effective as multiple injections, and is the most practical method for wide application.

In measles (rubeola) concentrated gamma globulin of human source is very effective in prevention of this disease if given after exposure. A good indication for prevention should be present, as this method provides passive protection for a short time only. The material is so effective that modification of the disease is difficult to be sure about if given before the onset of symptoms. Whether or not it will prevent measles encephalitis is not known.

The prevention or modification of whooping cough is possible when exposure is definite by the use of hyperimmune human serum. This substance plays a very useful role in the modification and therapy of infants suffering from whooping cough.

In summary, no known specific therapeutic agents are available for the treatment of the common viral respiratory tract infections. Penicillin, streptomycin, or sulfonamide drugs are useful in treating known bacterial infections when the organism is identified as a susceptible one. Postural drainage as an aid in preventing secondary bacterial disease is recommended, especially in infants and small children.

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Clinical Conference

CONFERENCE AT THE CHILDREN'S HOSPITAL OF MICHIGAN

DR. PAUL V. WOOLLEY, JR., PEDIATRICIAN-IN-CHIEF

Case 1. Methemoglobinemia Due to Well Water

DR. MARGARET DOWELL (Resident in Pediatrics).—This 18-day-old female baby was admitted on Feb. 17, 1948, because of cyanosis since the sixth day of life. She was born at a suburban hospital and apparently progressed well for five days, but soon after reaching home became blue and was returned to the hospital where she was kept in oxygen for five days before again being discharged. During the next few days she was said to have only intermittent attacks of cyanosis but on the day before admission she was irritable, passed several liquid stools, and required water between each feeding. During the day of admission the cyanosis reappeared and was more intense than ever before. It was learned during questioning of the parents that a sibling had been treated at this hospital three years ago for the same complaint, the cause of which was never determined.

Examination showed the baby to be husky but deeply cyanosed. The cyanosis was of the same intensity whether the infant was quiet or crying, in or out of oxygen. There was no cardiac enlargement or murmur, the lungs were clear and well aerated, and the liver was not enlarged. Both the pulse and respiratory rate were increased. Laboratory data, such as have been obtained, are of importance mainly in showing an initial hemoglobin concentration of 16 Gm. per cent, 7 Gm. of which was methemoglobin. Treatment on the day of admission was limited to the administration of 500 mg. of ascorbic acid intramuscularly and the repetition of this four hours later. A blood sample taken before the second injection showed a rise in oxyhemoglobin to 12 Gm. per cent and a determination the following morning revealed only 0.7 Gm. per cent of methemoglobin. The child at present appears entirely normal and happy, apparently none the worse for her experience.

DR. PAUL V. WOOLLEY, JR.—The resident staff is to be congratulated on its alertness with this case. The chart of the sibling was obtained, and when the diagnosis was found to have been methemoglobinemia of unknown etiology, treatment was immediately instituted for the present infant. Since attention lately has focused upon nitrates in well water as a common cause of methemoglobinemia, the parents were questioned concerning their habitat. They live rurally and obtain their drinking water from a shallow well; the same well was utilized when the other baby was sick. It is interesting, parenthetically, how often we stand on the brink of fame without falling or being pushed; the medical student who wrote the history on the first case devoted a complete paragraph to a description of the well and the salty taste of the water but followed the problem no farther.

Methemoglobinemia in general is not rare in pediatric practice and is usually associated with the ingestion, accidentally or therapeutically, or substances capable of serving as oxidizing agents. Recently we have shown instances where sulfadiazine, acetanilid, and Phenacetin have each been thought to be at fault. Formerly it was seen following cutaneous contamination with aniline and similar solvents then employed in shoe dyes and marking inks. It has even been suggested that the duskiness which characterizes certain instances of diarrhea in babies may be due to methemoglobinemia produced through the action of pyocyanin, the pigment of *Pseudomonas aeruginosa*. The role of nitrates has been known for years since these salts were introduced early as opaque media in gastrointestinal roentgenoscopy as well as in the treatment of enteritis. The common colon bacillus is able to reduce nitrates to nitrites and these, on absorption, undergo further reduction and thus serve as oxidizing agents. Nitrates, it will be recalled, occur in high concentration in certain immature surface waters and in this area we have now seen instances of poisoning from two separated communities and, according to the State engineers, there are other zones where nitrate well water is a potential hazard.

Treatment is usually dramatic and the mortality is low since cyanosis ordinarily appears before a critical reduction in oxyhemoglobin occurs. Methylene blue was long the reducing agent of choice but is now difficult to obtain, so that ascorbic acid has come into favor as a more readily available antidote. It is possibly a little slower in action than the dye, but, as illustrated by this case, is quite reliable.

QUESTION.—What happens to the hemoglobin during these various changes?

DR. LEONARD APT (Fellow in Hematology).—The iron in hemoglobin is usually present in the ferrous state and as such will combine with oxygen to form oxyhemoglobin. When exposed to oxidizing agents, the iron passes to a ferric state and is no longer capable of combining with oxygen. When reducing agents are introduced, the ferrous form is again active and once more combines with oxygen. Laboratory methods are available for both quantitative and qualitative estimations of methemoglobin. Methemoglobin can be readily differentiated from the reduced hemoglobin such as is seen in the cyanosis of congenital heart disease, since the latter combines readily with oxygen in the absence of a reducing substance.

FINAL NOTE

This patient was discharged on the day he was presented and the family was instructed to use city water until a new source could be developed. A sample of their water showed 974 parts per million of nitrates as compared with a safe level not in excess of 30 parts per million.

Case 2. Ratbite Fever Due to Streptobacillus Moniliformis

DR. MARGARET DOWELL.—This 3-year-old white boy was admitted May 11, 1948, because of chills and fever of one week's duration. One day before the onset of symptoms he had told his mother of having been bitten on the finger by a rat and she had noted a small puncture wound in the area indicated. The chills had occurred each evening and the fever had been present during the night with

usually only a minor elevation during the day. For three days before admission he refused to leave his bed although the mother could not ascribe this to any definite evidence of pain. The finger which had been bitten remained, during this period, only mildly inflamed and was not sore.

Upon admission he appeared acutely ill and cried constantly. His temperature was 102° F., pulse 136, and respirations 42. Marked swelling was noted about the right ankle which was also quite tender, and a second area of swelling occupied the region of the metacarpal phalangeal joints of the right hand. The middle finger of the left hand, where the bite was said to have occurred, showed two tiny puncture marks and minimal swelling of the distal phalanx; the lymph nodes in the left axilla, however, were swollen but not tender. Neither the liver nor the spleen was palpable, and nothing out of the ordinary could be detected in the chest. Over the trunk his skin was peppered with excoriated papules typical of scabies, but on the legs a different eruption was prominent—red, macular for the most part, with a tendency on the feet to form papules. Laboratory data obtained initially included normal urinalysis, negative Mazzini and tuberculin tests, and a white blood cell count of 14,000 per cubic millimeter with a predominance of polymorphonuclear leucocytes.

Early treatment was limited to the use of aspirin for control of pain and during the first four days his condition did not change. The fever was irregular but reached 102° F. each day and dropped to subnormal at the early morning recordings. The joints remained swollen and tender but new involvement did not appear. Several blood cultures were obtained and on the fourth day penicillin was administered with immediate response; his temperature has remained under 100° F., the joint swelling is subsiding, and his rash has disappeared. Typical growth of *Streptobacillus moniliformis* was observed in the earliest culture flask after five days' incubation.

DR. WOOLLEY.—It was not realized for a number of years that ratbite fever is really two unrelated diseases, one, the classical form (sodoku) due to *Spirillum minus*, the other, septicemia with *S. moniliformis*. The separation of these syndromes is usually accomplished quite easily although the possibility of them existing concomitantly must be kept in mind. Some of the more important points of divergence are as follows:

(a) The onset of sodoku follows an incubation period of about two weeks, and a chancroid exacerbation at the point of inoculation ushers in the clinical symptoms. The Haverhill (Streptobacillus) type does not have a clearcut incubation period but begins with fever a few hours or days after the bite. The point of inoculation in the latter disease may remain slightly inflamed from the start and I have never seen it resemble the chancre of sodoku.

(b) The course of sodoku is one of periodic elevation of temperature with two or more asymptomatic days between peaks. The bacterial form tends to a plateaued fever or to daily fluctuations. Joint involvement is part of the Haverhill variety but is rare or absent in spirillosis although muscle pains are not uncommon in the latter. A distinct macular rash is not unusual in the bacillary disease but evanescent blotches and blushes during fever are the typical manifestations of sodoku.

(c) Both diseases are characterized by mild leucocytosis, but positive reactions to precipitin tests, such as those of Kahn, Hinton, and Mazzini, are seen exclusively in sodoku. Moderate anemia is present in both as the infections persist.

(d) The diagnosis in Haverhill fever is made through the recovery of the streptobacillus from blood cultures; detection of the spirillum ordinarily requires injection of lymph node emulsion into animals, preferably guinea pigs.

Interestingly enough, both forms respond to penicillin. Arsenicals earlier gave satisfactory results. The prognosis in each is also excellent if treatment is instituted within a reasonable period. One little feature of streptobacillus infection is disturbing; that is the theoretic ease with which these patients can be confused on clinical grounds with the rheumatic fever-Still's disease group. Children are unreliable in giving information and many ratbites occur during sleep, so that it is quite possible to overlook the importance of a superficial cutaneous lesion. In areas such as ours, where rats are plentiful and their contacts with children frequent, we are most conscientious in obtaining blood cultures and utilizing therapeutic tests with penicillin. The same thing, I might add, applies to the possibility of confusing sodoku with congenital syphilis; we have had one baby admitted here as syphilitic because of fever, irritability, splenomegaly, and positive Mazzini test, who turned out to have ratbite fever.

DR. W. W. ZUELZER (Pathologist-in-Chief).—It remains a source of amazement that we are not more generally bothered by rat-borne diseases; I do not understand why Weil's disease is so rare in this hospital. It is important to remember that the Haverhill type of infection can be acquired without the bite of a rat. Outbreaks have been attributed to contaminated food and milk.

FINAL NOTE

Penicillin was stopped after seven days and the child has remained well.

Case 3. Congenital Obliteration of the Bile Ducts

DR. ROBERT W. MCCAMMON (Resident in Pediatrics).—This child is 15 months of age and was first admitted March 30, 1948, because of jaundice present since the ninth day of life. He is the third child in an otherwise normal family and was born after a supposedly uneventful pregnancy. Both jaundice and clubbing of the fingers were noted on the ninth day and the former has been progressively more severe. His early life was uneventful except for occasional bouts of diarrhea, and he gained steadily in size and weight. By 6 months of age he could sit, but since then development has continued more slowly so that while he crept at 11 months he still could not stand. His abdomen had become increasingly large, stools had always been light in color, and his urine was always dark and staining.

Examination showed him to be surprisingly well-nourished, weighing 21 pounds, and measuring 31.5 inches. His skin was bright lemon-yellow in color, and his mucous membranes were pale and stained. The anterior fontanel was widely patent and marked craniotabes was present. The fingers were definitely clubbed but the nails were not as thickened as is usually seen in cyanotic babies; the fingers did not seem sensitive nor irritated. There was a loud systolic mur-

mur over the precordium but it was soft in character, unaccompanied by a thrill, and free from sharp accentuation at any one point. The liver edge was 8 cm. below the costal margin and felt hard and rough, but no gross irregularities could be made out. The spleen also was enlarged, hard, and regular in outline. Essential laboratory data included an icteric index of 90, biphasic van den Bergh test, serum bilirubin 10 mg. per cent, and urine urobilinogen positive at 1:20 dilution but negative 1:30. A microcytic hypochromic anemia with hemoglobin of 3.2 Gm. per cent probably accounted for the heart murmur. The cephalin flocculation test was positive, but there was no reduction of prothrombin activity. X-ray studies of the long bones showed generalized rarefaction and low-grade rickets. Treatment during this first admission was limited to transfusions before he was removed by the parents who desired time to consider surgery.

He was readmitted two weeks later but had developed a severe upper respiratory infection which was complicated by diarrhea. He has now been returned to condition where surgery can be undertaken. It is interesting to note that since his anemia has been corrected, his color has changed from lemon yellow to a greenish yellow.

DR. WOOLLEY.—We are presenting this case in order to make a few points needing emphasis. First of all, it must be understood that we have no absolute method for diagnosing congenital defects of the biliary tract. Certainly progressive jaundice, increasing hepatomegaly, and absence of bile from the stools is most suggestive, especially if these continue until about 3 months of age. Exploration alone frequently does not provide a true answer. You have seen recently an infant who underwent laparotomy and in whom normal components of the biliary tract could not be identified. When Dr. Zuelzer presented the case at Pathologic Conference, following death during an outbreak of diarrhea, he demonstrated normal biliary structures and a healing of hepatitis. Exploration with the removal and examination of tissue affords the nearest approach to absolute diagnosis in doubtful instances. The clinical laboratory, while most helpful in ruling out certain confusable entities, does not possess a critical test in this condition.

Of the last dozen cases in which obliteration has been strongly suspected, the diagnosis has been confirmed on only three occasions. The remainder, on the basis of biopsy studies and/or clinical course, have been relegated to the heterogenous and poorly understood groups labelled hepatitis and cholangiolitis. This is surprising since Ladd[1] in his definitive contribution mentions icterus neonatorum, erythroblastosis, hemolysis due to sepsis, and syphilis as the only important differential worries. He does place great stress upon the role of inspissated bile in the ducts and possibly this is the point of confusion: is the bile inspissated and the larger passages empty because of dysfunction secondary to hepatitis or ascending infection, or does the inspissation per se cause the liver changes? This point deserves re-evaluation, especially when we remember that we are but a few years out of the catarrhal jaundice-mucous plug era; knowledge of hepatitis as an epidemic and infectious disease, and of homologous serum jaundice are mainly outgrowths of the recent war. Three of our recent "obliterations" have cleared up spontaneously before surgery could be performed and each gave a

history of progressive jaundice almost from birth, persisting for from six weeks to two months. The prognosis, so far as the present patient is concerned, is not good. I have little doubt from our findings and the history that he has an anomaly, and probably less than one in five of these are theoretically amenable to surgery. We have had only one cure in recent years, a girl shown in this clinic some months back who had a usable outpouching of duct which was successfully anastomosed to the duodenum. She is now quite normal in all respects.

I believe we can conclude that we must be chary in reaching a diagnosis of congenital atresia of the biliary tract and depend upon a history of progressive jaundice for at least three months, increasing hepatomegaly during the same period, and exploration with the examination of biopsy material. This is agreeable to the surgeons since they feel that the parts are better delineated by then and that permanent damage is not done the liver through reasonable delay. It is hardly necessary to stress that much more knowledge of liver disease in infancy would be highly desirable. Dr. Rosenzweig, what can you say about the clubbing?

DR. SAUL ROSENZWEIG (Senior Cardiologist).—Pediatricians associate clubbing with the cyanotic cardiacs but it is important to remember that it also appears in pulmonary disease and in liver dysfunctions associated with jaundice. I do not recall having seen it develop in a baby only 9 days of age.

QUESTION.—Would punch or needle biopsies assist in diagnosis?

DR. WOOLLEY.—These have been used rather extensively elsewhere but we feel much information is gained by laparotomy since the surgeon and pathologist can observe the organ grossly and choose representative areas for biopsy.

FINAL NOTE

This child was explored the following day. A rudimentary gall bladder and cystic duct were found but there was no trace of either common or hepatic ducts. The child is still living two months later, but we obviously have little to offer him.

Case 4. Meningitis Due to Hemophilus Influenzae

DR. RUDOLPH M. JARVI (Assistant Resident in Pediatrics).—This 1-year-old child entered the hospital May 26, 1948, because of fever for ten days and a convulsion shortly before arrival. He had always been well and had developed normally. He had been irritable when his fever was first noted, had seemed to have pain in one ear, and had vomited once. He was examined by a physician who prescribed conservative doses of sulfadiazine after finding an acute otitis media. During the next four days his temperature fell gradually and his other symptoms disappeared, so that for two days he seemed quite well and the sulfadiazine was discontinued. During the four days prior to admission, however, he appeared lethargic and listless although he was apparently not febrile. On the day of admission the mother said he felt warm, vomited, and had a generalized clonic convulsion.

His convulsion had stopped when he reached the hospital and he was listless and stuporous. His eyes were fixed and no attention was given his surroundings. The right eardrum was dull but not inflamed and the left appeared normal.

His throat was injected and although his neck and back were not rigid he resisted extreme flexion. There was nothing unusual in the examination of the chest or heart; his pulse rate was 120 per minute with a temperature of 101° F. Reflexes were generally hypoactive and in keeping with his posteonvulsive state. The laboratory data included normal urinalysis, white blood cell count elevated to 21,000 with a slight increase in the polymorphonuclear forms, a negative serology, and a negative reaction to tuberculin. Fluid obtained from a lumbar puncture was clear and under normal pressure but contained 128 white cells, of which 88 per cent were monocytic, and the protein was elevated to 102 mg. per cent. Sugar was present in the usual amount and no organisms were detected in stained preparations. X-ray films of the mastoids were interpreted by Dr. Evans as showing, "low-grade inflammatory reaction of some duration," and films of the chest revealed well-aerated lung tissue.

A convulsive episode in response to upper respiratory infection seemed the best possibility on admission, especially since examination after the child recovered from his posteonvulsive state still showed nothing pointing elsewhere. He was given both sulfadiazine and penicillin and later in the day sat up and took fluids eagerly. When the findings in the cerebrospinal fluid were recorded it was obvious that the initial impression was erroneous and attention was then focussed upon the possibility of an extradural process secondary to otitic infection; we still did not consider seriously a purulent meningitis. He slept well that night and on the following day sat in a high chair, smiled, and played. His temperature, however, remained elevated, and more cerebrospinal fluid was obtained. This contained 62 cells per cubic millimeter and again an elevated protein with normal sugar content. He was seen by an otorhinolaryngologist, who discounted the importance of any ear infection. There was no essential change in his condition during the next two hospital days except that the nurses felt, toward the end of this period, that he was a little more drowsy and irritable. His temperature remained elevated and tended to rise to higher levels than at admission. It was then that a report on the culture made from the second tap was obtained and showed group B, *Hemophilus influenzae*. Another lumbar puncture was done and by now the fluid was cloudy and contained over 400 cells with a predominance of polymorphonuclear forms; on the following day this had risen to 900 and the polymorphonuclear cells comprised 85 per cent. Treatment was changed by increasing the sulfadiazine, instituting streptomycin, omitting penicillin, and administrating specific rabbit antibody. Today he is but slightly febrile and appears, as you can see, comfortable and free from obvious neurologic signs.

DR. WOOLLEY.—Contrary to the findings in older children and adults, infants often show little physically upon which to make a diagnosis of meningitis; with some, as in this instance, even in retrospect it is difficult to point out when the central involvement took place and how it should have been detected. It is a rule in the emergency room here that no child be sent home after a "febrile" convulsion until a complete examination of the cerebrospinal fluid has been made; a convulsion associated with irritability and drowsiness is the most common history obtained in early influenza bacillus meningitis. Physically these infants often seem normal and apparently do not experience any great discomfort

nor exhibit classic signs of meningeal irritation; this, in our experience, is especially true of those in the age where the fontanel is open and the skull bones are not rigidly fixed. With the universal use of chemotherapy for all the ills of childhood, the problem has become even more exasperating since suboptimal amounts of the drugs will often hold progression in abeyance without effecting a cure. I believe it logical to consider seriously the possibility of an otitic spread after the initial fluid was examined although we usually can detect some localizing signs with a juxtadural process. We would be inclined now to discount the importance of the ears since Pfeiffer's bacillus more commonly involves that area as an extension of the mucous membrane infection and independent of the spread to the bloodstream with subsequent meningeal localization.

QUESTION.—How long will streptomycin be continued?

DR. WOOLLEY.—Our plan of treatment for influenza meningitis over the past two years has included sulfadiazine in amount sufficient to provide a blood level between 20 and 30 mg. per cent for at least seven days after cultures are sterile, antiserum early in the course, repeated if the power to "quell" is lost, and streptomycin for three days only. As you know, we use no intrathecal therapy except in the rare case where organisms persist for over three days and yet are biologically sensitive to one of the treatment agents. I do not recall resorting to this in the *H. influenzae* group but we have found it advisable to use intrathecal penicillin in one or two pneumococcic patients out of some twenty babies treated. We also use more antibody than is customary in most places since so many of our patients are seen late and since previous sulfadiazine therapy confuses our appraisal of the severity of infection. Streptomycin, in our experience, has not altered dramatically the outlook for influenza meningitis, so that we use it only in conjunction with the tried and true remedies, sulfadiazine and rabbit antibody. Dr. Zuelzer can speak with feeling on the brain damage which takes place with each succeeding day of infection and it therefore is our aim in all types of meningitis to strike with all our armament rather than testing clinically the efficacy of single therapeutic agents; this holds especially for the Pfeiffer bacillus where differences in individual susceptibility are strain characteristics. I would also like to point out that we treat purulent meningitis in infants as if due to *H. influenzae* until proved otherwise. This is based on two concepts: first, that the influenza bacillus is more likely to be hard to demonstrate than the gram-positive cocci or the colon group; and second, that the treatment, as outlined, is adequate for meningitis due to the meningococcus, whereas smaller doses of sulfadiazine and penicillin, as commonly effective in the meningococcic form, are of doubtful value in the influenzal type.

FINAL NOTE

This child made an uneventful recovery following the treatment as outlined and was discharged eleven days after presentation. He was seen a month later in the clinic and was continuing merrily along the curve of normal development.

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The Social Aspects of Medicine

FIRST ASSEMBLY OF THE WORLD HEALTH ORGANIZATION

During the last week of June and the early part of July, 1948, the First Assembly of the World Health Organization was held in Geneva. Some 450 delegates from sixty-nine nations were present to discuss and act on the agenda prepared by the Interim Commission. At the meeting, Dr. Andrija Stampar, rector of the University of Zagreb, Yugoslavia, was elected president, and Dr. Brock Chisholm, head of the Canadian Army's medical service during the war, director general.

Priority was given to the programs for malaria, tuberculosis, maternal and child health, venereal disease, and nutrition. Dr. Stampar is reported as holding the viewpoint that WHO should be primarily a clearing house for health information and a source of technical help in times of need, rather than a super health department above the health departments of the individual nations.

Parts of recommendations which were acted upon are of interest to pediatricians, particularly those relating to child and maternal health. The following is quoted from "Official Records of the World Health Organization, No. 10."

MATERNAL AND CHILD HEALTH

An international programme for maternal and child health is recommended in view of the high incidence of preventable deaths among infants and mothers in large areas of the world; the effectiveness of available techniques in reducing mortality and improving the health of infants and mothers; the immediate and continuing need, for the protection of coming generations, of scientific guidance in the utilization of available foodstuffs; the high incidence of communicable and other preventable diseases among children; the widespread mental and emotional maladjustment and insecurity among children and youth; the insufficient understanding and knowledge among parents and others of the causes of ill-health and abnormal behavior of children; and the effects of economic and social changes on the physical, mental and emotional development of children.

Objectives.—

To assist governments in developing services and facilities that will assure adequate maternity care, the best possible chance of survival to infants, and to all children normal physical growth and development, mental and emotional health, and freedom from preventable disease; to pool knowledge, acquire new facts, develop standards of care, and distribute information in respect of all relevant matters; and to cooperate with other agencies on joint undertakings which apply knowledge and techniques in the fields of social and biological sciences and of education to problems of maternity and childhood.

Programme.—

Studies on:

Statistical and other research projects on the causes and methods of reducing maternal, infant and childhood morbidity and mortality

Child guidance and mental health of children
Social aspects of a maternal and child health programme
Facilities and personnel for providing maternity care and health services for children, including hospital and auxiliary services.

Assistance to governments.—Provision of:

Expert advice on administration of maternal and child health programmes
Fellowships and visiting experts
Experts or teams to demonstrate special services.

Action on the international plane.—

A programme of co-operation and joint action with organizations concerned with maternal and child health
Collection and distribution of relevant information, including:
Results of research and investigations
Information on current procedures, methods and administrative practices
Preparation of reports on maternity and child care, including standard techniques, methods and practices, and materials for use in health education programmes.

Organization.—

A section on maternal and child health as part of the WHO Secretariat
An expert advisory committee consisting of not more than ten members, meeting say twice a year
A panel of corresponding members
Individual experts and teams, employed on a temporary basis as required.

Another matter of pediatric interest relates to international standards of biological products which is quoted as follows:

INTERNATIONAL STANDARDS

Therapeutic, Prophylactic and Diagnostic Agents.—

Biological standardization is a heritage from the Health Organization of the League of Nations, under whose auspices international standards and units have been established for thirty-nine substances which are assayed by biological methods. By agreement with the Danish Government and with the British Medical Research Council, the State Serum Institute, Copenhagen, and the National Institute for Medical Research, Hampstead, serve as centres for the preparation, maintenance and distribution of international standards.

Objectives.—To provide the medical practitioner with biological products of proved efficacy; to supply health authorities with standards for measuring the value of the biological remedies placed on the market; to simplify the task of the manufacturers who need to express the potency of export products only in terms of accepted international units.

It is proposed to develop a reference service library which will probably include the transfer of the library of the Office International d'Hygiene Publique, and of the medical and health sections of the former League of Nations Library. An expert library staff will be developed to meet requests made by national health administrations and health experts for bibliographic material.

An important question is the relationship of nongovernmental health organizations, which, for example, in the United States play such an important part in the national health field. The importance of such agencies is recognized,

but WHO is an organization of governmental agencies and is supported by government contributions. The following is the statement of principles as regard nongovernmental agencies:

STATEMENT OF PRINCIPLES

Criteria to be applied in placing Organizations on the List of Non-governmental Organizations eligible to be brought into Relationship with WHO under Article 71 of the Constitution.

The WHO should, in relation to non-governmental organizations, act in conformity with any relevant resolutions of the General Assembly of the United Nations, and the following criteria should be met before an organization can be regarded as eligible to be brought into relationship:

(i) The organization shall be concerned with matters falling within the competence of the World Health Organization.

(ii) The aims and purposes of the organization shall be in conformity with the spirit, purposes and principles of the Constitution of the World Health Organization.

(iii) The organization shall be of recognized standing and shall represent a substantial proportion of the persons organized for the purpose of participating in the particular field of interest in which it operates. To meet this requirement, a group of organizations may form a joint committee or other body authorized to act for the group as a whole.

(iv) The organization shall have authority to speak for its members through its authorized representatives; evidence of this authority shall be presented if requested.

(v) The organization shall normally be international in its structure, with members who exercise voting rights in relation to its policies or action.

(vi) Save in exceptional cases, a national organization which is affiliated to an international non-governmental organization covering the same subject on an international basis shall present its views through its government or through the international non-governmental organization to which it is affiliated. A national organization may, however, be included in the list, after consultation with the Member State concerned, if the activities of the organization are not covered by any international organization or if it offers experience upon which the World Health Organization wishes to draw.

Comments on Current Literature

THE TREATMENT OF HAVERHILL FEVER

IT IS now fairly well established that fever following ratbite may be caused by either of two etiologic agents: *Spirillum minus* or *Streptobacillus moniliformis*. These two organisms, so different biologically, produce similar clinical pictures. The disease due to *Spirillum minus* is produced only by the bite of a rat or some other animal carrying the organism. On the other hand, septicemia due to *Streptobacillus moniliformis* results from ratbite, or may follow the ingestion of contaminated material.

Knowledge of *Streptobacillus moniliformis* dates from 1914 when Schottmüller, investigating a case of fever following ratbite, isolated from blood cultures an organism which he termed *Streptothrix muris ratti*. Within the next decade a similar organism was recovered in several instances from the blood of patients during febrile course following ratbite. In 1925 Levaditi, Nicolau, and Poincloux[1] named the organism *Streptobacillus moniliformis*.

The disease is characterized by abrupt onset with chills, fever, vomiting, and headache, following an average incubation period of about six days. There is characteristically an early maculopapular rash, frequently resembling that of rubella, and present mainly on the extremities. Arthritis, which is typically present, may be severe and may involve many joints. A characteristic fever curve has been described, rising abruptly at first with remission in from two to five days, followed by recurrence with arthritic symptoms. The white blood cell count may be normal, but as a rule is elevated.

In January, 1926, an epidemic of unusual fever occurred in Haverhill, Mass. Place, Sutton, and Willner[2] (1926) described the clinical findings and later in the same year the bacteriology of this epidemic was reported in detail by Parker and Hudson.[3] Clinical findings corresponded well with those reported following ratbite, but none of these cases was associated with ratbite. From blood and joint fluid of some of these patients Parker and Hudson recovered a highly pleomorphic organism which proved to be gram-negative, and required serum for its growth in artificial medium. The source of the epidemic was traced to a dairy distributing unpasteurized milk. Believing this to be a new disease and a newly identified organism, these investigators termed the disease Haverhill fever (erythema arthriticum epidemicum) and the organism, *Haverhillia multiformis*. It is now felt that these organisms, reported independently, are the same. Cultured with a fair degree of ease from blood or joint fluid, the organism is described as a slender, gram-negative, non-acid-resisting rod which is highly pleomorphic and stains with difficulty. Irregularity of form is characteristic: swellings and enlargements; tendencies to form threads and toward branching. Fermentation of some carbohydrates occurs, and in general the organism requires blood or ascitic fluid for growth.

While the diagnosis of Haverhill fever is not especially difficult, therapy has presented a difficult problem. Until penicillin became available, no form of therapy seemed to be effective. This is in contrast to the excellent results obtained in ratbite fever due to *Spirillum minus*, where response to therapy with arsenicals is favorable. In the case of *Streptobacillus moniliformis*, gold salt in the form of gold sodium thiomalate was thought to be effective in controlling experimental infection in mice, but its use in the treatment of infections in human subjects did not give dramatic response.

Since the introduction of penicillin, successful treatment by its use has been reported in a number of cases. Certain patients, however, particularly those with chronic infections and long-standing joint involvement, fail to respond to penicillin.

A recent issue (June, 1948) of the *Proceedings of the Society for Experimental Biology and Medicine* carries an interesting report by Jennie S. Levey and Stanley Levey.[4] In an attempt to obtain information concerning the efficacy of various therapeutic agents, these investigators undertook a study of experimental infection of mice with *Streptobacillus moniliformis*. Evaluation of therapeutic agents was made by allowing inoculated mice to develop swollen joints before attempting therapy. The organism used was the Manning strain of *Streptobacillus moniliformis* isolated from the blood of a patient who developed severe arthritis. This strain proved extremely virulent for mice, swollen joints resulting as early as forty-eight hours following inoculation, and many mice succumbing at this time. Routine broth cultures were followed simultaneously with each group of inoculated mice. The agents tested were penicillin G, streptomycin, Myochrysine (gold sodium thiomalate), Solganal B (gold thioglucose in oil), sulfathiazole, para-aminosalicylic acid, para-aminobenzoic acid, Promizole, Promin and methylene blue. Therapy was initiated three days after the first appearance of joint swelling. Evaluation of therapy was based on complete disappearance grossly of all joint involvement. The results of these studies, summarized by the authors in the following table, are of considerable interest.

TABLE I. EFFECT OF VARIOUS AGENTS UPON JOINT INVOLVEMENT PRODUCED BY STREPTOBACILLUS MONILIFORMIS

GROUP	DRUG	COURSE OF THERAPY	NO. OF ANIMALS TESTED	NO. OF ANIMALS CURED	PER CENT CURED
1	Control		63	1	1.6
2	Penicillin G	10,000 units I.P. 3× daily, 4 days	32	12	37.5
		1,000 units I.P. 3× daily, 6 days	16	11	69.0
3	Streptomycin	5,000 units I.P. 3× daily, 3 days	7	6	85.0
		2,500 units I.P. 3× daily, 3 days	17	13	76.0
4	Myochrysine	1.25 mg. I.V. every other day, 10 doses	17	0	0
		5 mg. I.P. single dose	5	0	0
		4.0 mg. I.V. every other day, 10 doses	8	0	0
5	Solganal-B in oil	10 mg. I.M. single dose	7	0	0
6	Sulfathiazole	1 % in diet, 38 days	11	0	0
7	p-Aminosalicylic acid	.5% in diet, 9 days	13	0	0
8	p-Aminobenzoic acid	.4% in diet, 21 days	10	0	0
9	Promizole	.5% in diet, 5 days	13	1(?)	0
10	Methylene blue	.2% in diet, 20 days	5	0	0
11	Promin	.5% in diet, 21 days	22	0	0

Of sixty-three controls, only one survived; penicillin G proved effective in 37½ per cent in one group of mice and in 69 per cent in another group; streptomycin proved more effective than penicillin for this strain of the organism, 76 per cent in one group and 85 per cent in another. Remission of joint involvement was more prompt in the streptomycin-treated mice. In a discussion of their results, Levey and Levey refer to a report by Sprecher and Copeland[5] in 1947. This is a case report on a patient with severe joint manifestations who was treated with penicillin for six days without remission, but who showed dramatic improvement following the third dose of streptomycin. Sprecher and Copeland suggest that variability in strain susceptibility may be an important factor involved.

The experimental study by Levey and Levey seems to bear out the general clinical impression that penicillin is effective in combatting infections with

Streptobacillus moniliformis but to a lesser degree than streptomycin. However, with the idea of strain diversity in mind, as well as drug toxicity, it is suggested that a combination of the two forms of therapy might yield the most satisfactory clinical results.

Evaluation of the newer antibiotics in the therapy of Haverhill fever must await experimental studies and adequate clinical trial.

RUSSELL J. BLATTNER.

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News and Notes

Preliminary plans are being made for the next International Pediatric Congress which will be held at Zurich, Switzerland, in August, 1950.

Dr. Leonard Davidson has been appointed Professor of Pediatrics and head of the Department at the University of Louisville Medical School. Dr. James W. Bruce has been appointed Clinical Professor of Pediatrics.

Correspondence

London, England
July 12, 1948

The Meeting of the British Paediatric Association took place this year at Windermere on April 16, and it was with the greatest pleasure that we welcomed Dr. Henry Helmholz, a Corresponding Member of our Association, who had been invited to deliver the first Windermere Lecture. This is a specially endowed lectureship, and Dr. Helmholz chose as his subject "Milk, a European Child Health Problem." The lecture, which was excellent, will be published in due course. All of us were delighted to have him with us, and those who had attended the International Paediatric Congress in New York last July were especially pleased that Dr. Helmholz, who was President of the Congress, was able to attend our meeting. We recalled the hospitality that had been accorded to us in the United States and the generosity of the American Committee that had made the trip possible for many of us, and we were all most happy to do what we could in this country for our distinguished visitor. The meeting had a record attendance, but as the proceedings will be published shortly, no further details are called for here.

During the past twelve months the most important events, affecting paediatricians as well as all other members of the medical profession, have been concerned with the proposed National Health Service, which actually came into effect on July 5 of this year.

As I am sure that this whole affair has received very full attention in American medical journals already, I do not propose to go into any details, but I must refer to certain salient points of this very important matter. In my last letter I commented upon what appeared to be a split in the profession over the National Health Service Act, arising from a divergent point of view between the general practitioner and his interests on the one hand, and the consultant and specialist, whose work is so largely bound up with hospital work and the teaching of medicine, on the other. Most of us felt, however, that a unified professional front was vital, and in the course of arguments and meetings in connection with this Act, it happily emerged that despite some difference in professional interests, the over-riding principle of professional freedom was all that really mattered, and that the consultants would, therefore, stand in with their general practitioner colleagues and support them in opposition to the Act as originally laid down. In view of all the circumstances, the British Medical Association decided to hold a plebiscite in February of this year so as to determine the position taken up by the profession as a whole on this vital issue.

The results of this plebiscite were very striking. There was an 84 per cent poll of the whole medical profession in Britain. Of those voting (38,534), 90 per cent expressed disapproval of the Act as it then stood; of 17,626 general practitioners (out of a total of 19,345 voting) who expressed disapproval, 17,037 also voted against accepting service. Of the consultants and specialists there were nearly 10 to 1 against. One of the most surprising things was the result of the voting of those who were themselves engaged in whole-time government service; of these, 634 disapproved and only 127 expressed their approval of the Act.

Such figures make it quite clear how strong was the feeling against the Act as it then stood. The Minister of Health was made aware by these figures of the strength of the opposition, and he was also given to understand that it was a fear of the introduction of a whole-time salaried service that was a chief course of widespread apprehension and opposition.

On April 7, 1948, the Minister stated in the House of Commons that he was prepared to introduce an Amending Act whereby it would be made impossible for him to introduce a whole-time, state-salaried service except by further direct Act of Parliament, that he would explicitly allow complete freedom of publication even in criticism of the service by those engaged in it, and he also undertook to modify the basic salary in such a way as to meet the views of the general practitioner.

These concessions were of such an order as to alter the picture in a very material way, for they went very far toward assuring that professional freedom which we were so determined to preserve. Following the Minister's announcement the British Medical Association felt, very properly in view of the February plebiscite, that another vote should be taken in the light of the fresh position which had thus been created. This second plebiscite was held in April, and 40,622 medical men and women out of a total of 54,724 voted. Of these, 25,842 still expressed disapproval of the Act, but in view of the concessions offered by the Minister, the numbers in favour of accepting service and of trying to make a success of it was now almost equal to those opposed to entering the Service, and among these opponents there were only 9,588 general practitioners as compared with more than 17,000 who adopted such an attitude in the February plebiscite.

Quite clearly, in view of this swing-over of opinion, there no longer existed a strong united opposition to the Act, and the Council of the British Medical Association accordingly advised the profession to accept service under the Act as it will be amended.

There is general relief that a head-on collision has been avoided, and that following what was undoubtedly a great victory for the profession, concessions on both sides opened up the way to cooperation.

Further confirmation of the improved nutrition of children over here comes in the second study of the teeth of young school children, carried out by May Mellanby and Helen Coumoulos. It shows that the dental health of 5-year-old school children examined in 1943 was much better than that of the 1929 group, and that there was a still further appreciable improvement in 1945; a point of special significance is that the percentage of carious teeth showing arrest of the disease was almost twice as large in 1945 as in 1943. It is suggested that this state of affairs was due to the increased calcifying properties of the dietary of this country.

In March the Prime Minister announced that the Government had accepted the recommendations of the Curtis and Clyde Committees, and that a single central department concentrated in the Home Office should be made responsible for providing a home background for children deprived of a normal home life. The primary function of the Children's Branch of the Home Office would be to ensure that everything possible is done to give homeless children not only material care, but also the sense of security and status that the normal home provides. This is one of the most important and outstanding advances of a social paediatric nature that has come to pass in recent years.

During the last year we have suffered here from the most severe epidemic of acute anterior poliomyelitis ever experienced in this country. The corrected notifications of cases will probably total about 7,500, giving an attack rate of 3.8 per 100,000 population. One of the striking features was the higher age incidence of the patients, 34.9 per cent being aged 15 years and over. The mortality increased with age, from a minimum of 3.2 per cent at the ages of 1 to 4 years up to 34.7 per cent in persons aged 45 years and over. As shown in an important contribution by Ritchie Russell, physical activity in the preparalytic stage was definitely related to an increased severity of the subsequent paralyses.

(Signed) K. H. TALLERMAN.

Book Reviews

An Account of the Weather and Diseases of South Carolina. Lionel Chalmers, M.D., London, 1776.

This small booklet is made up of extracts from the writings of Dr. Lionel Chalmers of Charles-Town, S. C., which were published in 1776 in two volumes under the above title. Some fifty-odd of the 446 pages of the original text were concerned with pediatric subjects. These have been selected for reproduction by Dr. Joseph I. Waring, and reprinted in a small brochure by Mead Johnson & Company as a souvenir of the Centennial of the South Carolina Medical Association which was held in March, 1948. Dr. Waring contributes a short biography of Dr. Chalmers, who was born in Scotland in 1715, and came to Charleston in 1735, where he practiced until his death in 1777.

It is interesting historically, as it gives an excellent picture of the ideas held 200 years ago as to the causation of disease and the methods of treatment at that time. Included are discussions of such subjects as "worms," "convulsions," "thrush," and the "hooping-cough," whose epidemic nature is clearly described.

Studies on Child Development. Arnold Gesell, M.D., New York, 1948, Harper and Brothers, 224 pages. Price $4.00.

A collection of essays and addresses which in large part have been presented from time to time by invitation before medical and scientific groups. All are concerned with child development and there is a definite continuity in the arrangement and selection. The reviewer has obtained from the book a much broader and more comprehensive picture of the work of the Yale Clinic of Child Development than he held from the separate reading of the numerous books by Dr. Gesell on individual phases of these studies. It is beyond question that Dr. Gesell's work in the field of child development is one of the outstanding contributions to pediatrics in our time. In this volume the reader obtains a picture of the breadth of his interests. The pediatrician who is chiefly familiar with such studies from the Yale Clinic as "Developmental Diagnosis" will find particular interest in some of the chapters, which are in reality summaries of some of the less familiar studies of a more psychologic nature as "twin control," the essay on the conditioned reflex, and "genius and growth." The volume is good reading and will add a breadth of viewpoint to the physician working with children.

Nursing for the Poliomyelitis Patient. Prepared and published by the Joint Orthopedic Nursing Advisory Service of the National League of Nursing Education. (To all of which should be added that the preparation and publication was financed by the National Foundation for Infantile Paralysis.)

All of these organizations should be given full credit for rendering a real service by contributing to the preparation of this unusually excellent handbook of eighty-eight pages covering in detail the various phases and problems of caring for the patient with poliomyelitis. It is well written and the description of techniques and procedures are expressed in simple, clear-cut language.

While the book is primarily intended for the nurse, it is a book that every physician who has the responsibility for the care of a patient with poliomyelitis can read with profit to himself and to his patient. While the procedures described in the book are to be carried out by the nursing service, the physician is ultimately responsible for the nursing care and must have a knowledge of the nursing procedures. With the increase in the incidence of the disease this year the brochure is unusually timely.

Copies may be secured by writing the National Foundation for Infantile Paralysis, 120 Broadway, New York 5, N. Y.

Editor's Column

A REPREHENSIBLE PETTY MEDICAL GRAFT

IN RECENT months the newspapers and lay magazines have contained numerous discussions of the "kickbacks" on eyeglasses which have finally ended in court proceedings, and whose acceptance by some ophthalmologists has brought disgrace upon the entire medical profession.

Our attention was directed a few weeks ago to another form of medical graft, petty by comparison, the sale of "professional samples." Post cards were received by St. Louis physicians from an individual in Chicago offering to buy the free samples left at our offices, and stating he would make a personal call to buy them. He also stated he had been in the "business" for a number of years.

Perhaps we live in the clouds but this was a new racket to us, although obviously it was one of some years' standing in several communities. A little investigation revealed that it is a well-organized business, and that in certain communities pickup trucks are used to carry on the work. Further, it seems there is no legal redress to stop it. In New York City, we understand, samples by law must carry the statement "Professional Sample—not to be sold," but seemingly this has little effect.

We are concerned about it as the pediatrician receives many times the samples received by practitioners in other fields, and many nonmedical items come to him in the way of foods for use in infant feeding. The selling of these professional samples is a despicable form of petty graft that is inexcusable and can only lead to the lowering of personal as well as medical standards. It offers a temptation to the young physician just starting in who has great trouble in making both ends meet, as refunds for glasses did for the young ophthalmologist. We feel that it is a serious breech of the high ethical and moral standards which the physician must hold, and individuals guilty of such practices should be expelled from our medical societies for unethical conduct in that they bring the entire profession in disrepute.

The blame cannot all be placed on the medical profession as the samples are thrust upon the physician by the commercial houses whether the doctor wants them or not. A large part comes unrequested through the mail and most of these promptly and frequently unopened find a place in the wastebasket. What becomes of these wastebasket samples in a large medical office building might well be investigated. Another large part stems from the polite and affable detail man who ends his talk by asking if he cannot send samples. It is so much easier and quicker to say "yes" rather than "no," even if the samples are not wanted. And so the closet shelf rapidly becomes filled with samples that sooner or later must be disposed of, in part at least, to make room for still more. In fact, as every pediatrician knows, the sample business can at times become an actual nuisance.

Perhaps a committee of pediatricians and the firms who furnish the samples could get together and work out some way to regulate the distribution of samples and the racket, which, if continued, cannot fail to lower the dignity and standing of the medical profession. Certainly we know of no more brazen example of contempt for the ethical standards of the physician than this open proposal to purchase "professional samples."

B. S. V.

CHILD HEALTH AND LONGEVITY

No more striking example of the effect of the child health movement in the United States can be found than in the tables of the average life expectancy in 1946, which have recently been issued by the National Office of Vital Statistics.

The average length of life at birth for a female white child born in 1946 was 70.3 years, and if she lived to be one year old, was 71.3. The white male infant had an expectancy of some five years less, the figures being 65.1 and 66.6, respectively. For nonwhite the figures are some seven and one-half years less for the male infant and nine years less for the female infant at birth.

This steady and continuing increase in the average life expectancy has been brought about chiefly by the steady decline of the infant mortality rate during the last forty years, and by control of the infectious diseases by specific preventive measures in the last twenty-five years. In the last decade the treatment of the respiratory and blood stream infections by chemical and antibiotic drugs has been a contributing factor favorably influencing the average length of life.

The average white male 65 years of age will live to be 77.6 years old, and the female of 65 to be 79.5. Thus pediatrics has led to geriatrics and a whole new set of medical, social, and economic problems.